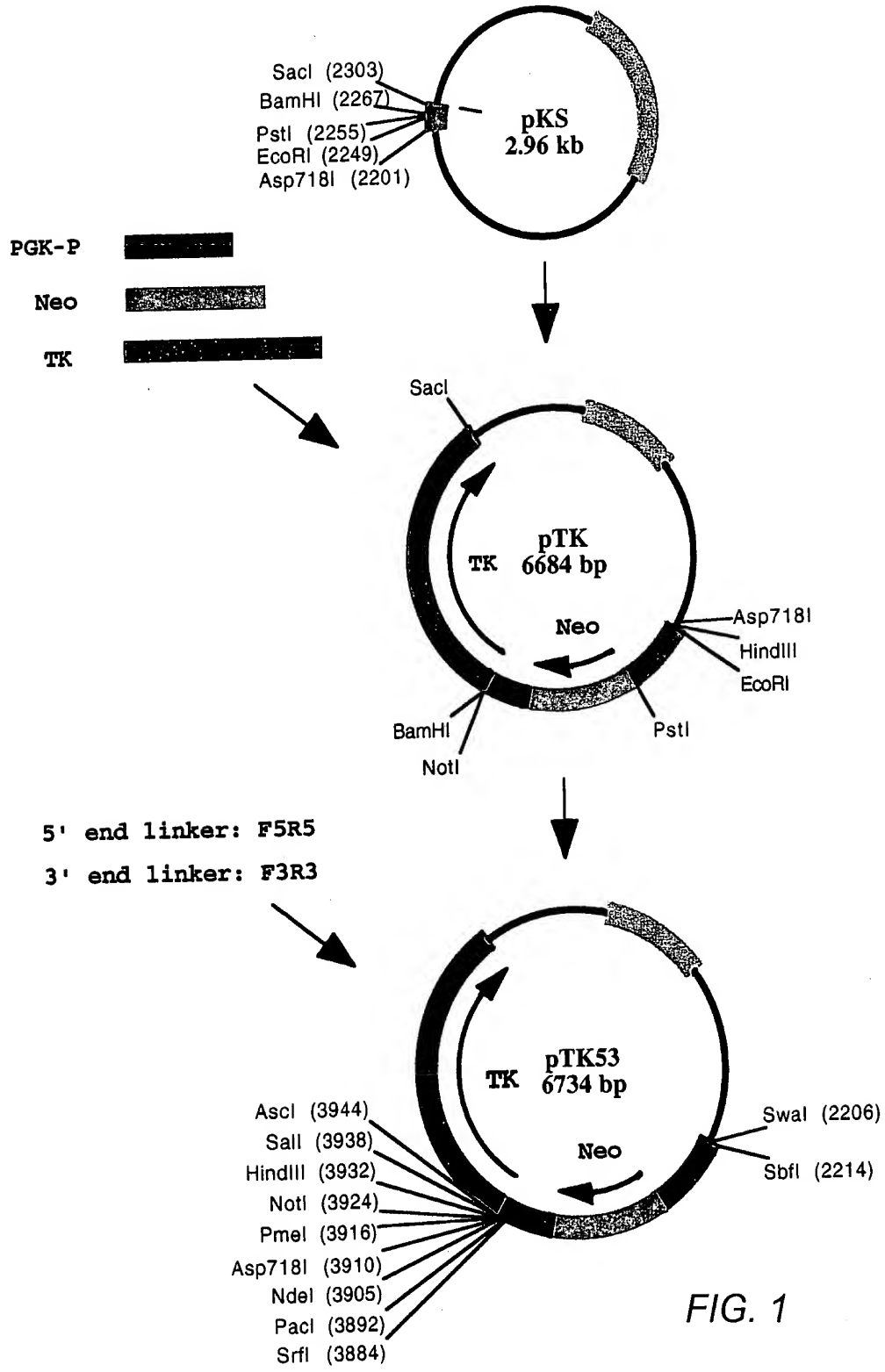
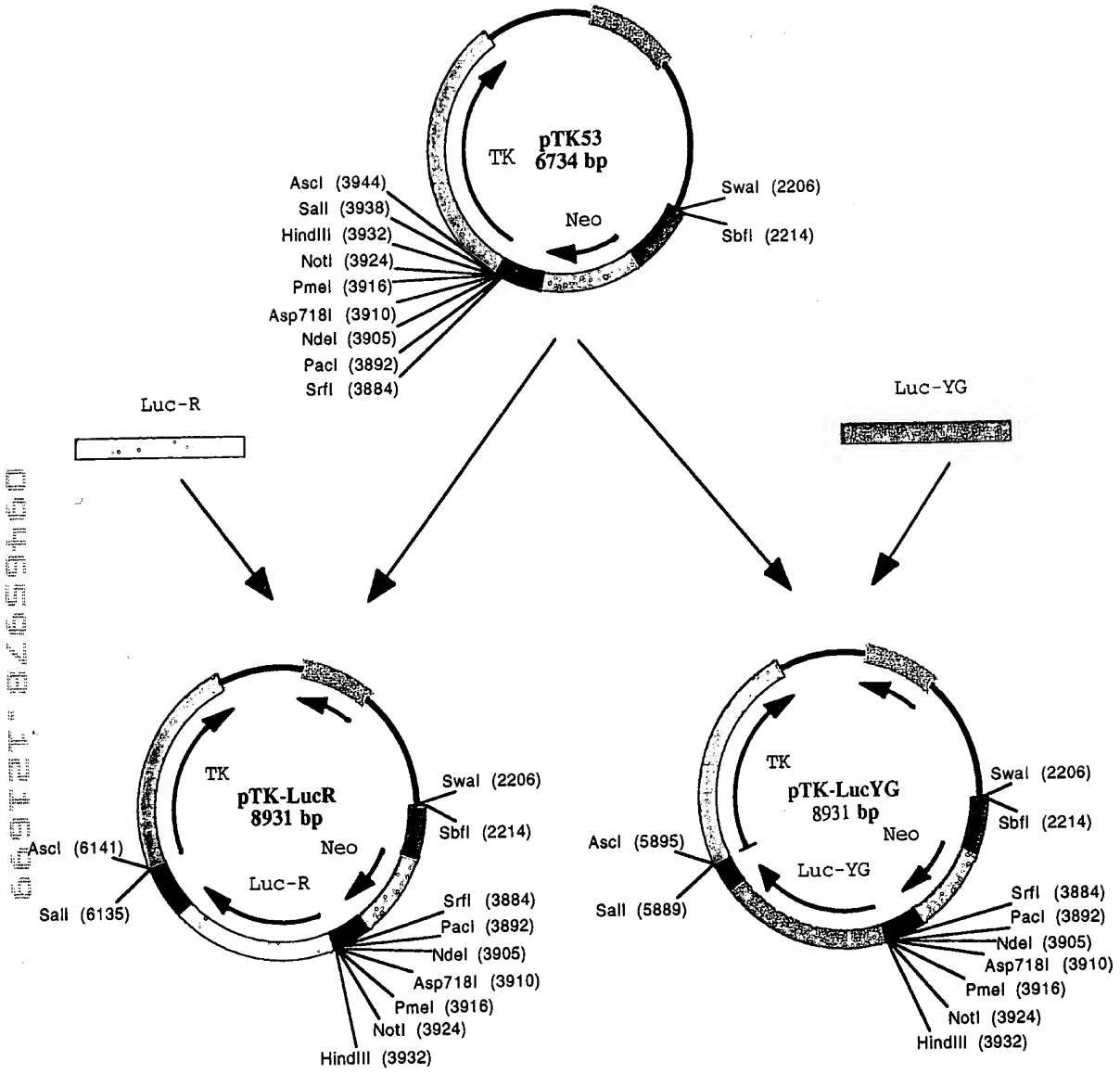

SacI (2303)
BamHI (2267)
PstI (2255)
EcoRI (2249)
Asp718I (2201)
pKS
2.96 kb
PGK-P
Neo
TK
SacI
pTK
TK 6684 bp
Neo
Asp718I
HindIII
EcoRI
BamHI
NotI
PstI
5' end linker: F5R5
3' end linker: F3R3
pTK53
TK 6734 bp
Neo
AscI (3944)
SalI (3938)
HindIII (3932)
NotI (3924)
PmeI (3916)
Asp718I (3910)
NdeI (3905)
PacI (3892)
SrfI (3884)
SwaI (2206)
SbfI (2214)

FIG. 1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6734 bp
TK
Neo
AscI (3944)
SalI (3938)
HindIII (3932)
NotI (3924)
PmeI (3916)
Asp718I (3910)
NdeI (3905)
PacI (3892)
SrfI (3884)
SwaI (2206)
SbfI (2214)
Luc-R
Luc-YG
pTK-LucR
8931 bp
AscI (6141)
SalI (6135)
pTK-LucYG
8931 bp
AscI (5895)
SalI (5889)

FIG. 2

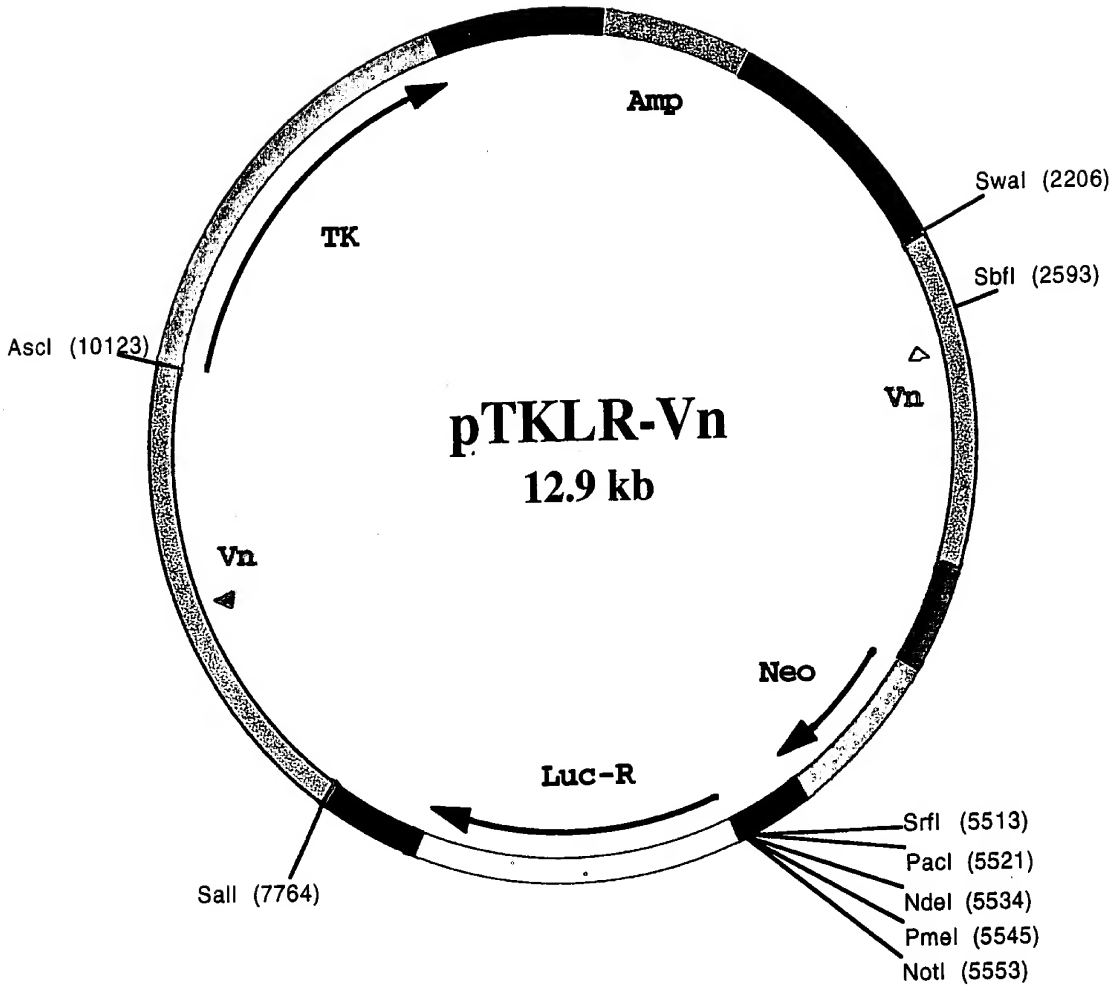

Amp
SwaI (2206)
SbfI (2593)
Vn
Neo
Luc-R
SrfI (5513)
PacI (5521)
NdeI (5534)
PmeI (5545)
NotI (5553)
SalI (7764)
Vn
AscI (10123)
TK
pTKLR-Vn
12.9 kb

FIG. 3A

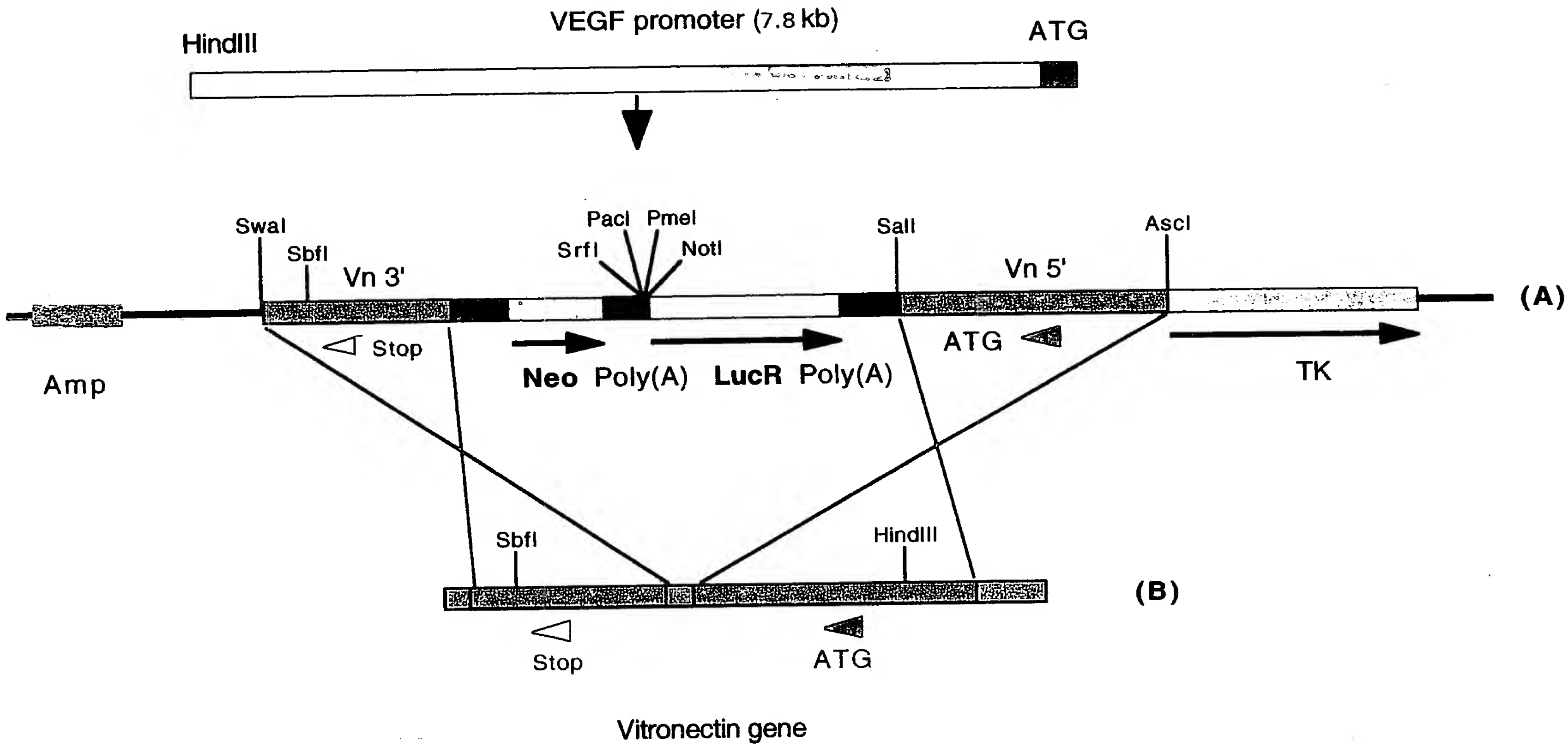
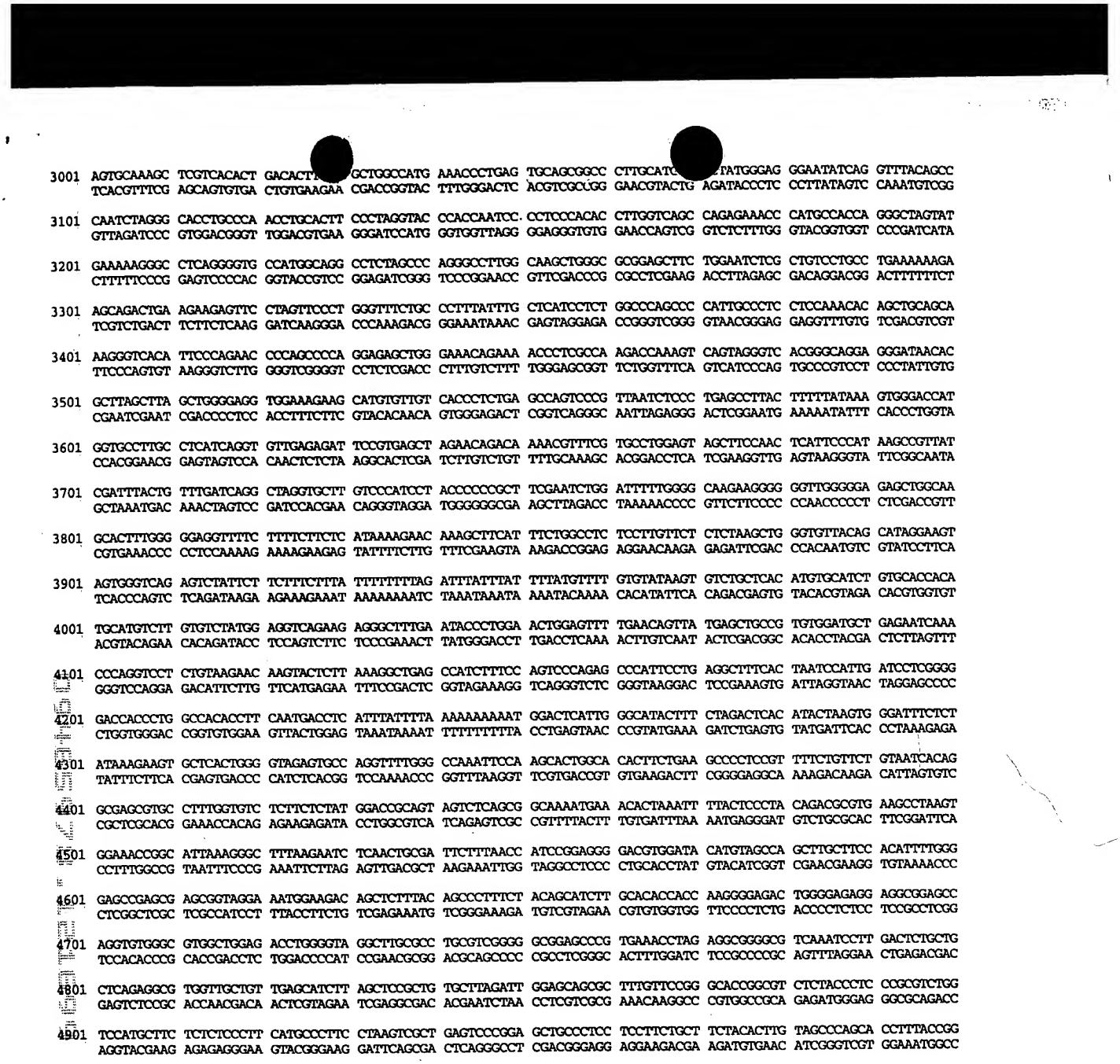


FIG. 3B

FIG. 3C-1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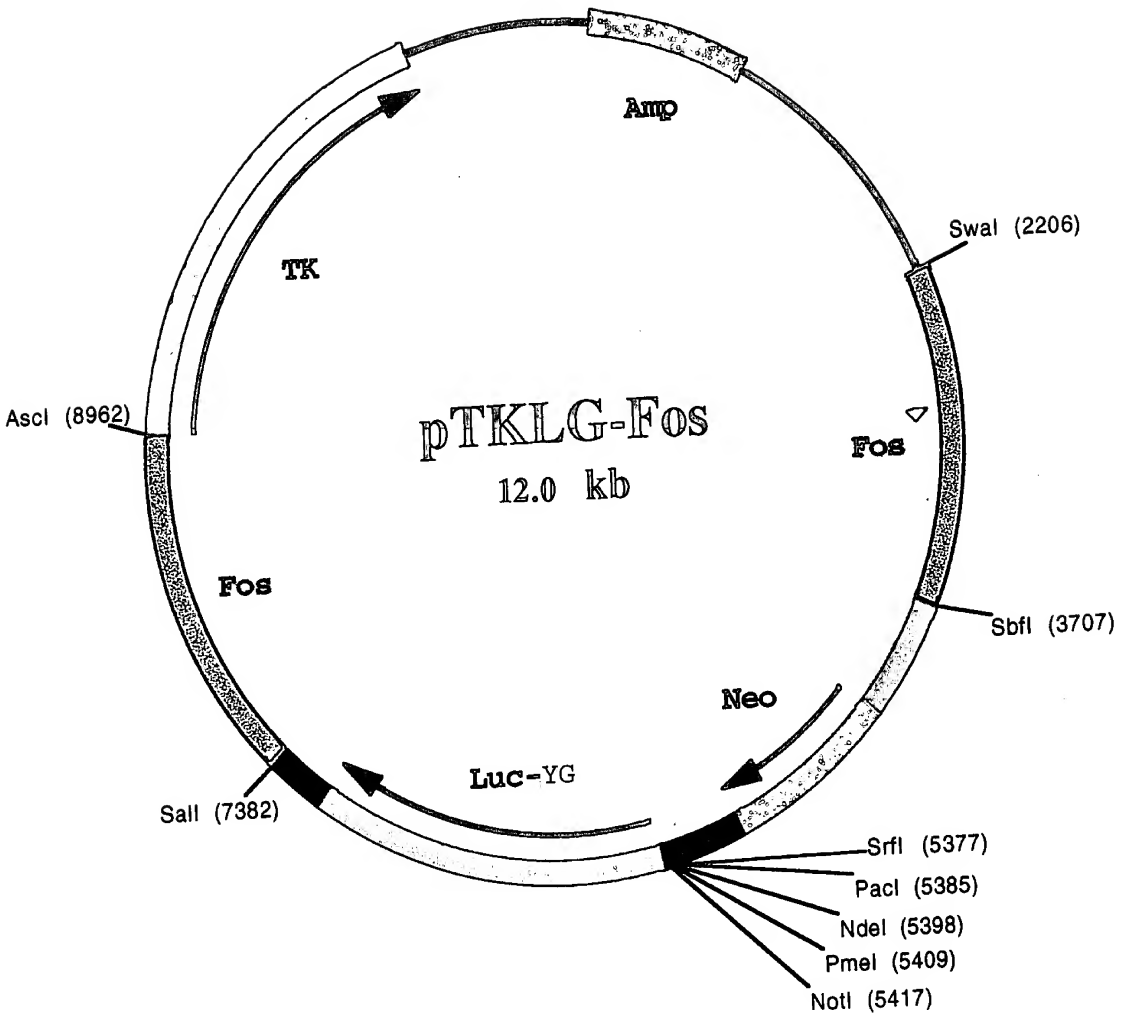
TCACGTTTCG AGCAGTGTGA CTGTGAAGAA CGACCGGTAC TTTGGGACTC ACGTCGCCGG GAACGTACTG AGATACCCTC CCTTATAGTC CAAATGTCGG
3101 CAATCTAGGG CACCTGCCCA ACCTGCACTT CCCTAGGTAC CCACCAATCC CCTCCCACAC CTTGGTCAGC CAGAGAAACC CATGCCACCA GGGCTAGTAT
GTTAGATCCC GTGGACGGGT TGGACGTGAA GGGATCCATG GGTGGTTAGG GGAGGGTGTG GAACCAGTCG GTCTCTTTGG GTACGGTGGT CCCGATCATA
3201 GAAAAAGGGC CTCAGGGGTG CCATGGCAGG CCTCTAGCCC AGGGCCTTGG CAAGCTGGGC GCGGAGCTTC TGGAATCTCG CTGTCCTGCC TGAAAAAAGA
CTTTTTCCCG GAGTCCCCAC GGTACCGTCC GGAGATCGGG TCCCGGAACC GTTCGACCCG CGCCTCGAAG ACCTTAGAGC GACAGGACGG ACTTTTTTCT
3301 AGCAGACTGA AGAAGAGTTC CTAGTTCCCT GGGTTTCTGC CCTTTATTTG CTCATCCTCT GGCCCAGCCC CATTGCCCTC CTCCAAACAC AGCTGCAGCA
TCGTCTGACT TCTTCTCAAG GATCAAGGGA CCCAAAGACG GGAAATAAAC GAGTAGGAGA CCGGGTCGGG GTAACGGGAG GAGGTTTGTG TCGACGTCGT
3401 AAGGGTCACA TTCCCAGAAC CCCAGCCCCA GGAGAGCTGG GAAACAGAAA ACCCTCGCCA AGACCAAAGT CAGTAGGGTC ACGGGCAGGA GGGATAACAC
TTCCCAGTGT AAGGGTCTTG GGGTCGGGGT CCTCTCGACC CTTTGTCTTT TGGGAGCGGT TCTGGTTTCA GTCATCCCAG TGCCCGTCCT CCCTATTGTG
3501 GCTTAGCTTA GCTGGGGAGG TGGAAAGAAG CATGTGTTGT CACCCTCTGA GCCAGTCCCG TTAATCTCCC TGAGCCTTAC TTTTTATAAA GTGGGACCAT
CGAATCGAAT CGACCCCTCC ACCTTTCTTC GTACACAACA GTGGGAGACT CGGTCAGGGC AATTAGAGGG ACTCGGAATG AAAAATATTT CACCCTGGTA
3601 GGTGCCTTGC CTCATCAGGT GTTGAGAGAT TCCGTGAGCT AGAACAGACA AAACGTTTCG TGCCTGGAGT AGCTTCCAAC TCATTCCCAT AAGCCGTTAT
CCACGGAACG GAGTAGTCCA CAACTCTCTA AGGCACTCGA TCTTGTCTGT TTTGCAAAGC ACGGACCTCA TCGAAGGTTG AGTAAGGGTA TTCGGCAATA
3701 CGATTTACTG TTTGATCAGG CTAGGTGCTT GTCCCATCCT ACCCCCCGCT TCGAATCTGG ATTTTTGGGG CAAGAAGGGG GGTTGGGGGA GAGCTGGCAA
GCTAAATGAC AAACTAGTCC GATCCACGAA CAGGGTAGGA TGGGGGGCGA AGCTTAGACC TAAAAACCCC GTTCTTCCCC CCAACCCCCT CTCGACCGTT
3801 GCACTTTGGG GGAGGTTTTC TTTTCTTCTC ATAAAAGAAC AAAGCTTCAT TTCTGGCCTC TCCTTGTTCT CTCTAAGCTG GGTGTTACAG CATAGGAAGT
CGTGAAACCC CCTCCAAAAG AAAAGAAGAG TATTTTCTTG TTTCGAAGTA AAGACCGGAG AGGAACAAGA GAGATTCGAC CCACAATGTC GTATCCTTCA
3901 AGTGGGTCAG AGTCTATTCT TCTTTCTTTA TTTTTTTTAG ATTTATTTAT TTTATGTTTT GTGTATAAGT GTCTGCTCAC ATGTGCATCT GTGCACCACA
TCACCCAGTC TCAGATAAGA AGAAAGAAAT AAAAAAAATC TAAATAAATA AAATACAAAA CACATATTCA CAGACGAGTG TACACGTAGA CACGTGGTGT
4001 TGCATGTCTT GTGTCTATGG AGGTCAGAAG AGGGCTTTGA ATACCCTGGA ACTGGAGTTT TGAACAGTTA TGAGCTGCCG TGTGGATGCT GAGAATCAAA
ACGTACAGAA CACAGATACC TCCAGTCTTC TCCCGAAACT TATGGGACCT TGACCTCAAA ACTTGTCAAT ACTCGACGGC ACACCTACGA CTCTTAGTTT
4101 CCCAGGTCCT CTGTAAGAAC AAGTACTCTT AAAGGCTGAG CCATCTTTCC AGTCCCAGAG CCCATTCCTG AGGCTTTCAC TAATCCATTG ATCCTCGGGG
GGGTCCAGGA GACATTCTTG TTCATGAGAA TTTCCGACTC GGTAGAAAGG TCAGGGTCTC GGGTAAGGAC TCCGAAAGTG ATTAGGTAAC TAGGAGCCCC
4201 GACCACCCTG GCCACACCTT CAATGACCTC ATTTATTTTA AAAAAAAAAT GGACTCATTG GGCATACTTT CTAGACTCAC ATACTAAGTG GGATTTCTCT
CTGGTGGGAC CGGTGTGGAA GTTACTGGAG TAAATAAAAT TTTTTTTTTA CCTGAGTAAC CCGTATGAAA GATCTGAGTG TATGATTCAC CCTAAAGAGA
4301 ATAAAGAAGT GCTCACTGGG GTAGAGTGCC AGGTTTTGGG CCAAATTCCA AGCACTGGCA CACTTCTGAA GCCCCTCCGT TTTCTGTTCT GTAATCACAG
TATTTCTTCA CGAGTGACCC CATCTCACGG TCCAAAACCC GGTTTAAGGT TCGTGACCGT GTGAAGACTT CGGGGAGGCA AAAGACAAGA CATTAGTGTC
4401 GCGAGCGTGC CTTTGGTGTC TCTTCTCTAT GGACCGCAGT AGTCTCAGCG GCAAAATGAA ACACTAAATT TTACTCCCTA CAGACGCGTG AAGCCTAAGT
CGCTCGCACG GAAACCACAG AGAAGAGATA CCTGGCGTCA TCAGAGTCGC CGTTTTACTT TGTGATTTAA AATGAGGGAT GTCTGCGCAC TTCGGATTCA
4501 GGAAACCGGC ATTAAAGGGC TTTAAGAATC TCAACTGCGA TTCTTTAACC ATCCGGAGGG GACGTGGATA CATGTAGCCA GCTTGCTTCC ACATTTTGGG
CCTTTGGCCG TAATTTCCCG AAATTCTTAG AGTTGACGCT AAGAAATTGG TAGGCCTCCC CTGCACCTAT GTACATCGGT CGAACGAAGG TGTAAAACCC
4601 GAGCCGAGCG AGCGGTAGGA AATGGAAGAC AGCTCTTTAC AGCCCTTTCT ACAGCATCTT GCACACCACC AAGGGGAGAC TGGGGAGAGG AGGCGGAGCC
CTCGGCTCGC TCGCCATCCT TTACCTTCTG TCGAGAAATG TCGGGAAAGA TGTCGTAGAA CGTGTGGTGG TTCCCCTCTG ACCCCTCTCC TCCGCCTCGG
4701 AGGTGTGGGC GTGGCTGGAG ACCTGGGGTA GGCTTGCGCC TGCGTCGGGG GCGGAGCCCG TGAAACCTAG AGGCGGGGCG TCAAATCCTT GACTCTGCTG
TCCACACCCG CACCGACCTC TGGACCCCAT CCGAACGCGG ACGCAGCCCC CGCCTCGGGC ACTTTGGATC TCCGCCCCGC AGTTTAGGAA CTGAGACGAC
4801 CTCAGAGGCG TGGTTGCTGT TGAGCATCTT AGCTCCGCTG TGCTTAGATT GGAGCAGCGC TTTGTTCCGG GCACCGGCGT CTCTACCCTC CCGCGTCTGG
GAGTCTCCGC ACCAACGACA ACTCGTAGAA TCGAGGCGAC ACGAATCTAA CCTCGTCGCG AAACAAGGCC CGTGGCCGCA GAGATGGGAG GGCGCAGACC
4901 TCCATGCTTC TCTCTCCCTT CATGCCCTTC CTAAGTCGCT GAGTCCCGGA GCTGCCCTCC TCCTTCTGCT TCTACACTTG TAGCCCAGCA CCTTTACCGG
AGGTACGAAG AGAGAGGGAA GTACGGGAAG GATTCAGCGA CTCAGGGCCT CGACGGGAGG AGGAAGACGA AGATGTGAAC ATCGGGTCGT GGAAATGGCC

FIG. 3C-2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12.0 kb
Amp
TK
Fos
Fos
Neo
Luc-YG
AscI (8962)
SwaI (2206)
SbfI (3707)
SalI (7382)
SrfI (5377)
PacI (5385)
NdeI (5398)
PmeI (5409)
NotI (5417)

FIG. 4A

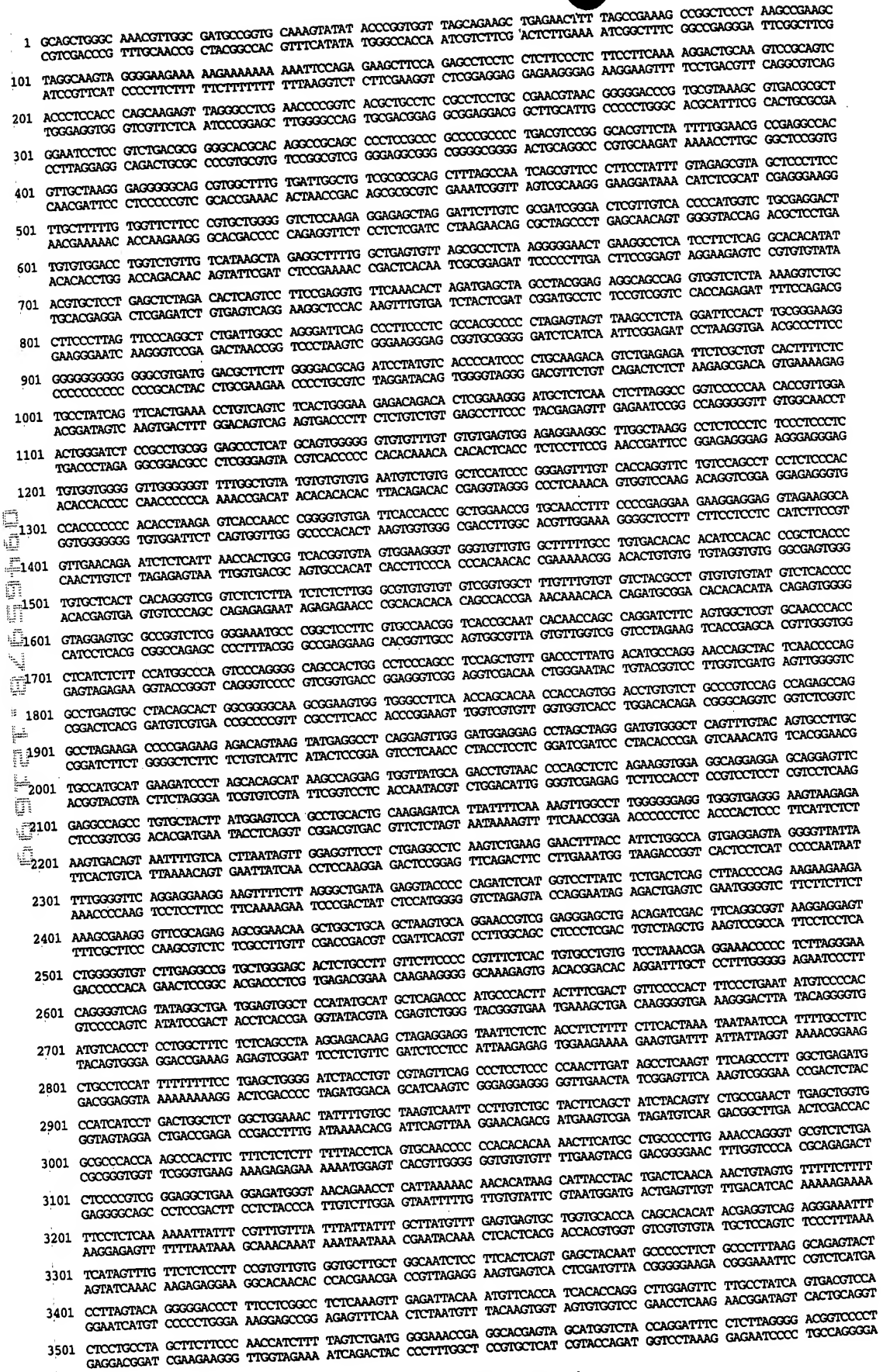

FIG. 4B-1

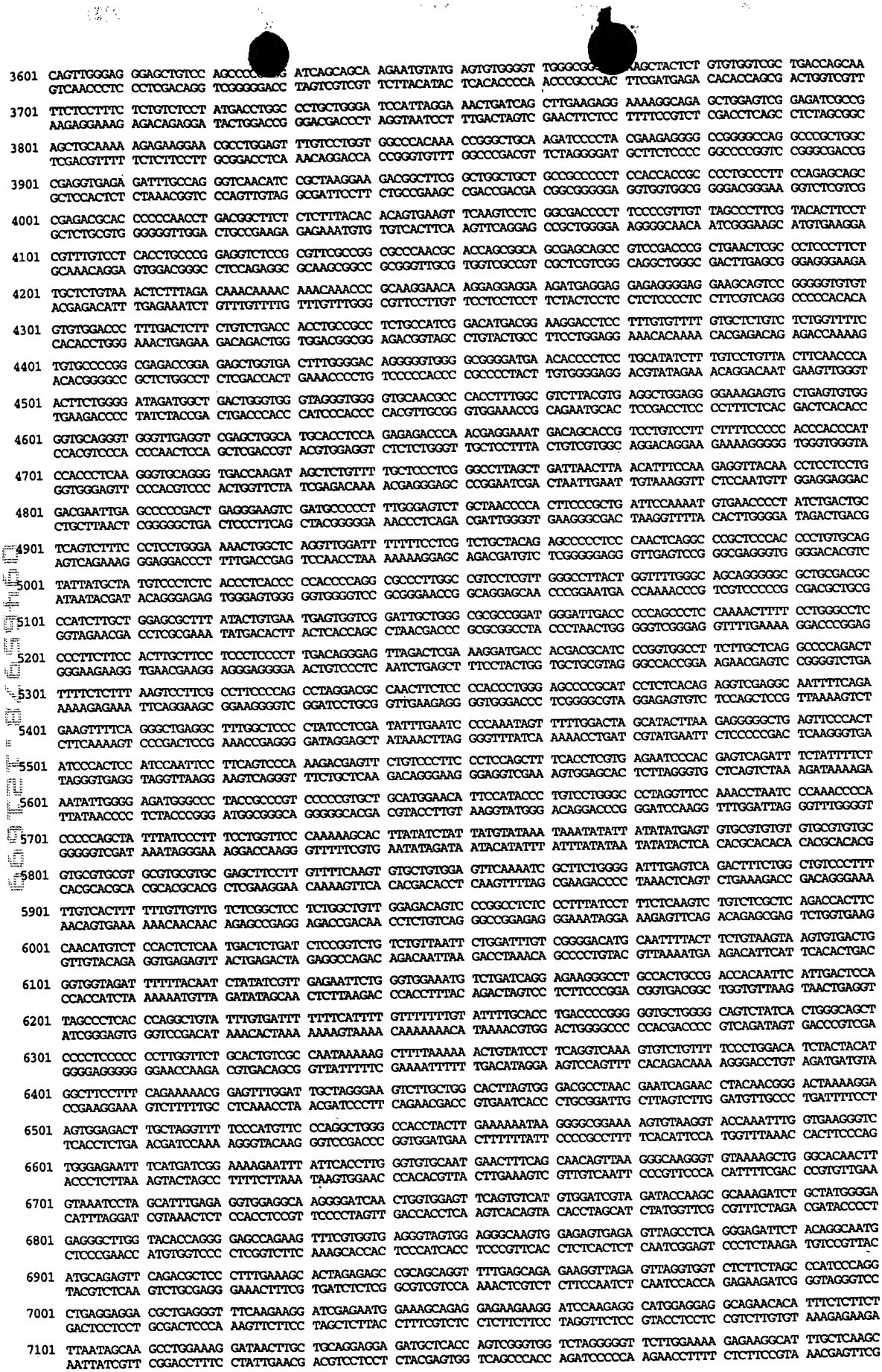

FIG. 4B-2

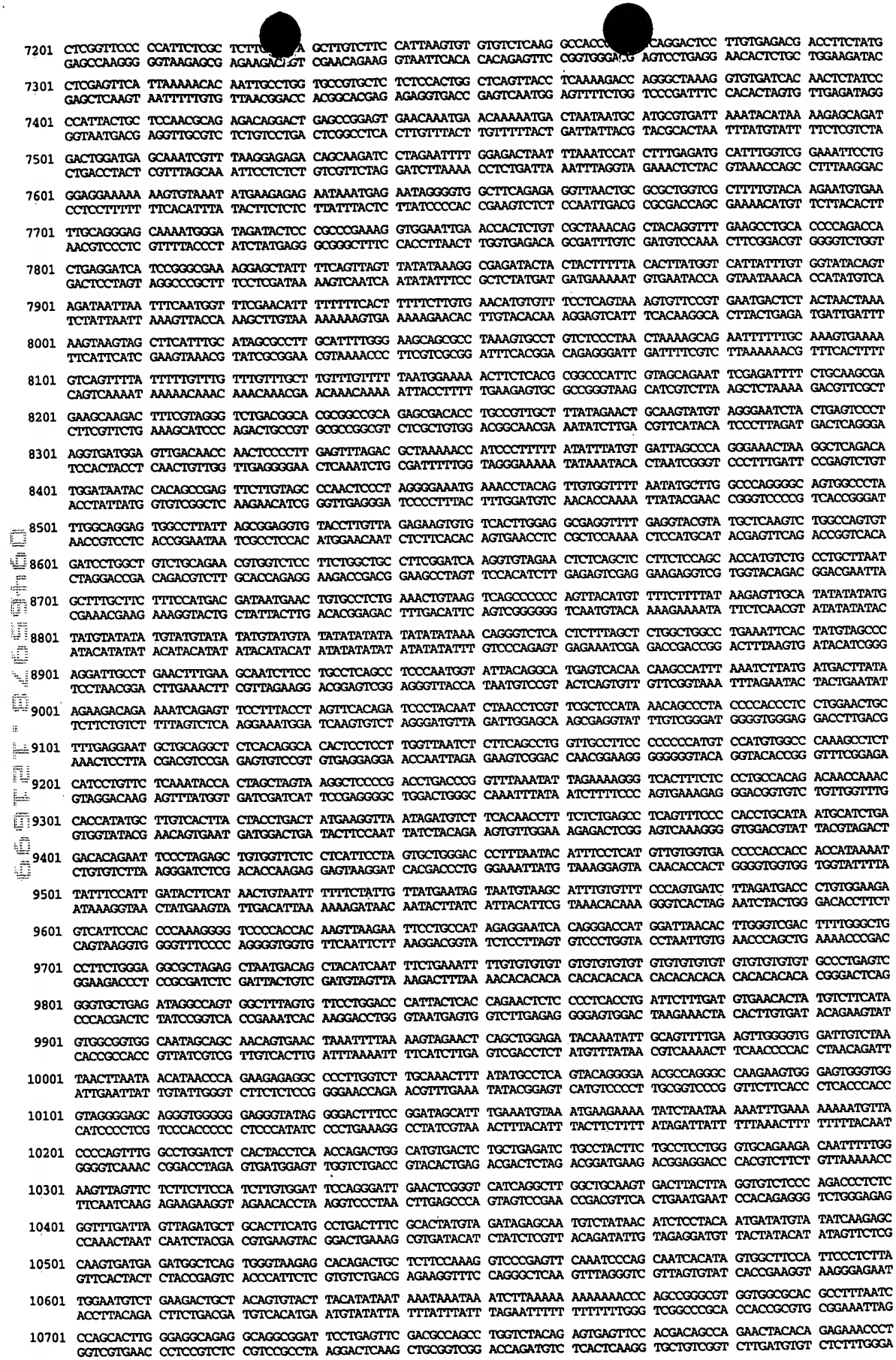

FIG. 4B-3

10801 GTCTCGAAAA AAAAAAGAGA GAGAG[illegible]G TGAGAGCGCA ATAATCTTAA CATTTCTGTG GTTGTC[illegible]TGTAGTCTA TTCTGATAAG CAATGCTGGC
CAGAGCTTTT TTTTTTCTCT CTCTCCCTTC ACTCTCGCGT TATTAGAATT GTAAAGACAC CAACAGAAAC GACATCAGAT AAGACTATTC GTTACGACCG

10901 TTGCTCCCAA GGTAGGAAGT AACATTTCTT TATAAAAGGT ATTTGCTCTG CTTTATTTTT CTGTTTTATT TATGGTGCTG AGGATGGAAC CCAGGACCCT
AACGAGGGTT CCATCCTTCA TTGTAAAGAA ATATTTTCCA TAAACGAGAC GAAATAAAAA GACAAAATAA ATACCACGAC TCCTACCTTG GGTCCTGGGA

11001 TGGCAAGCAA GGCTAGCTGT TTACCACTGA GCCATACTCC AGCCTTGCAC TGGGGGATTC TAGGCAAGGG TTCTACCACT GAGCCACACT CCCCACCCCC
ACCGTTCGTT CCGATCGACA AATGGTGACT CGGTATGAGG TCGGAACGTG ACCCCCTAAG ATCCGTTCCC AAGATGGTGA CTCGGTGTGA GGGGTGGGGG

11101 ATCCCTCTCT GGAAGATTCT AGGCAGTTCC ATACCTAGCC TTTGATCTTT TAAGACGGTC TTACTAGAGC TCAGTT
TAGGGAGAGA CCTTCTAAGA TCCGTCAAGG TATGGATCGG AAACTAGAAA ATTCTGCCAG AATGATCTCG AGTCAA

FIG. 4B-4

```
        10        20        30        40        50        60        70        80        90       100
AAGCTTGCAGGGAGGTAGGAGGCAGCCTGTGGCGTTGATTCAATGCACCTGGCCTTATCCTCGGATGAGATCGGTCACCAGTCAAAAACTGTGAGCTTGA
TTCGAACGTCCCTCCATCCTCCGTCGGACACCGCAACTAAGTTACGTGGACCGGAATAGGAGCCTACTCTAGCCAGTGGTCAGTTTTTGACACTCGAACT

       110       120       130       140       150       160       170       180       190       200
AGGTCTTGGGTGCTTAACATCTATTTTTACAAATCTTATTTAGCAACTTAGAACTGTGAAATATTGGAAAGCTACTTAAACCTTCTAAACTCCCTCCTCC
TCCAGAACCCACGAATTGTAGATAAAAATGTTTAGAATAAATCGTTGAATCTTGACACTTTATAACCTTTCGATGAATTTGGAAGATTTGAGGGAGGAGG

       210       220       230       240       250       260       270       280       290       300
ACACTATGAGAATGTTACATTTTCTATTCAGTTATTTTTGAGCAGTAAACAGATGAATCAAGGAATATGCCCATCACATCAAGAGTGCTCCTAAATGGAC
TGTGATACTCTTACAATGTAAAAGATAAGTCAATAAAAACTCGTCATTTGTCTACTTAGTTCCTTATACGGGTAGTGTAGTTCTCACGAGGATTTACCTG

       310       320       330       340       350       360       370       380       390       400
TTGCTTGTTATTCATTTACAGTGTGGCCCCTTGACTTTCATCGGCACTCCTAGCAGAAAACAAAATCCGCCAGATGGAGCTGGAGAGATGGCTCAGCTGT
AACGAACAATAAGTAAATGTCACACCGGGGAACTGAAAGTAGCCGTGAGGATCGTCTTTTGTTTTAGGCGGTCTACCTCGACCTCTCTACCGAGTCGACA

       410       420       430       440       450       460       470       480       490       500
TAAGAATACTTATCCCTACACAGGCCCTGGAGCCAGTTCCCAGCACCCACACGGTGGCTCACAACCATCTGTAACTCCAGTTCTAGGAGACCCGACTCCC
ATTCTTATGAATAGGGATGTGTCCGGGACCTCGGTCAAGGGTCGTGGGTGTGCCACCGAGTGTTGGTAGACATTGAGGTCAAGATCCTCTGGGCTGAGGG

       510       520       530       540       550       560       570       580       590       600
TCTTCTGTCTGAAAACACCAGGCACGCGTGCGGCTACATACAAACATGAAAGCAAAATACACACATTACATAAATAAATCTTAAAAAATGATTCGGGGTG
AGAAGACAGACTTTTGTGGTCCGTGCGCACGCCGATGTATGTTTGTACTTTCGTTTTATGTGTGTAATGTATTTATTTAGAATTTTTTACTAAGCCCCAC

       610       620       630       640       650       660       670       680       690       700
GGGGAAGGAAAAAAAAAGGATGTTAGAAAATCGATGTAACTGTTTTTTCCTTTTGCACAGATCTAAGTAGGGAAGGAGAACATTCTCTTACCATCGAGAAT
CCCCTTCCTTTTTTTTTCCTACAATCTTTTAGCTACATTGACAAAAAAGGAAAACGTGTCTAGATTCATCCCTTCCTCTTGTAAGAGAATGGTAGCTCTTA

       710       720       730       740       750       760       770       780       790       800
AATTGTTTTCATTGCCCCCAAGTCTGCTAATAGAGCTTGCTACCTTCATGGCTGTCGTAAGGATGAGGCAAAGATGGACTTCAGCTTTCAGACTGTGTCT
TTAACAAAAGTAACGGGGGTTCAGACGATTATCTCGAACGATGGAAGTACCGACAGCATTCCTACTCCGTTTCTACCTGAAGTCGAAAGTCTGACACAGA

       810       820       830       840       850       860       870       880       890       900
GCTCAAATGTTGGCTACTCCTGTTTTCTGACCCCCTTCTCTGGTGCAATGTGGACTTTCAATTAATTTCCCTGCATCTTTTACATATTTGATTTAAAAAA
CGAGTTTACAACCGATGAGGACAAAAGACTGGGGGAAGAGACCACGTTACACCTGAAAGTTAATTAAAGGGACGTAGAAAATGTATAAACTAAATTTTTT

       910       920       930       940       950       960       970       980       990      1000
TATTTTATTTTATGTAATTGTATGTATATGCATGTCAATAAGCATATGTGTGTGTGTTTCCATGGAAACCAAGGCAACAGATTCTCCAGAGCTGTAGAAA
ATAAAATAAAATACATTAACATACATATACGTACAGTTATTCGTATACACACACACAAAGGTACCTTTGGTTCCGTTGTCTAAGAGGTCTCGACATCTTT

      1010      1020      1030      1040      1050      1060      1070      1080      1090      1100
TGGGCTGTGAGACGCCCACTGTGGGTGCTCGGAACCAAACTCGGGTCCTGTGGAAAGACAGCGAGCACCCATAATGCAGAGGTATCTCTCAGACTCTACT
ACCCGACACTCTGCGGGTGACACCCACGAGCCTTGGTTTGAGCCCAGGACACCTTTCTGTCGCTCGTGGGTATTACGTCTCCATAGAGAGTCTGAGATGA

      1110      1120      1130      1140      1150      1160      1170      1180      1190      1200
TTAAAATTTCAATTTATCTTTTTTTTTTTTTAAAGTTCCAAGTAACTATAGGAAAGTACATGGGTATATAGATCCCCAGTACCAAGATTCTTCCTTTGCAG
AATTTTAAAGTTAAATAGAAAAAAAAAAAAATTTCAAGGTTCATTGATATCCTTTCATGTACCCATATATCTAGGGGTCATGGTTCTAAGAAGGAAACGTC

      1210      1220      1230      1240      1250      1260      1270      1280      1290      1300
GTAGCACAACTTGGTCTGCTTCACATAAAGAATGGAAAGTCATTAAAACACTCATCACACTGTAAAGTAGAATTGAACTCTGACAGAACAAGCGAAGTGA
CATCGTGTTGAACCAGACGAAGTGTATTTCTTACCTTTCAGTAATTTTGTGAGTAGTGTGACATTTCATCTTAACTTGAGACTGTCTTGTTCGCTTCACT

      1310      1320      1330      1340      1350      1360      1370      1380      1390      1400
GTCTGACTTCCAGGTAACTGAGCCTTCTTTTCCTCCTAAAGACACAAGCCATACACAGAGTAAAATAAACTTGGGCATGGTGAGAAGGAAACAACGCAGG
CAGACTGAAGGTCCATTGACTCGGAAGAAAAGGAGGATTTCTGTGTTCGGTATGTGTCTCATTTTATTTGAACCCGTACCACTCTTCCTTTGTTGCGTCC

      1410      1420      1430      1440      1450      1460      1470      1480      1490      1500
AGGGCTAGCCAAGTCTGAGAGTCGTGAGTGTGCTCGGTTTATAAACGGAGCCCACCTTGCCAGCGAGGTAGTCACATGCTCTGCTAAACAGAAACTTAAG
TCCCGATCGGTTCAGACTCTCAGCACTCACACGAGCCAAATATTTGCCTCGGGTGGAACGGTCGCTCCATCAGTGTACGAGACGATTTGTCTTTGAATTC

      1510      1520      1530      1540      1550      1560      1570      1580      1590      1600
AAAACACTTACACGAAGCAAACATGGGGAAGTGCCATGCAAGCATGTGACTGACTGGTGGCAATGACCGAAACCACAGCAGCCACTAGAAAAGGAAGGGT
TTTTGTGAATGTGCTTCGTTTGTACCCCTTCACGGTACGTTCGTACACTGACTGACCACCGTTACTGGCTTTGGTGTCGTCGGTGATCTTTTCCTTCCCA

      1610      1620      1630      1640      1650      1660      1670      1680      1690      1700
AGTGCGCCACACTGTAGTTGTGAAAATGAACTTATTCATTTATTTTGAAAAACGTGTAAGAAGCAAAGATGTCTTCTTTCCCACCTACCTTTGCGGCAGG
TCACGCGGTGTGACATCAACACTTTTACTTGAATAAGTAAATAAAACTTTTTGCACATTCTTCGTTTCTACAGAAGAAAGGGTGGATGGAAACGCCGTCC

      1710      1720      1730      1740      1750      1760      1770      1780      1790      1800
CGAGCACTTCCTGGAATTTATAAAGTGCGATCTTTCTGGGGACTTCTCATAACATTTCCTACTGCTCATCTATGTCTGTGTCAAATAGAGAATGCTCTTG
GCTCGTGAAGGACCTTAAATATTTCACGCTAGAAAGACCCCTGAAGAGTATTGTAAAGGATGACGAGTAGATACAGACACAGTTTATCTCTTACGAGAAC

      1810      1820      1830      1840      1850      1860      1870      1880      1890      1900
AACAAGTGTGTGTGTGTGTGTGTGTGCGCGCGCACGCGCACTCACTCCTGCTCTGTTGAGGTCCAGTTTTGATGGTCCCGCCAGAGGTATATTTGAGTAT
TTGTTCACACACACACACACACACACGCGCGCGTGCGCGTGAGTGAGGACGAGACAACTCCAGGTCAAAACTACCAGGGCGGTCTCCATATAAACTCATA

      1910      1920      1930      1940      1950      1960      1970      1980      1990      2000
CATTTCTCAAGAGCTTCAGCTGGGAGACACTGCCTCTTACTGGCCTGAAGGTCACTAGCTGATTCATCTCCGTTTGGGCTGGCGCGCCTTGGGGATCCTC
GTAAAGAGTTCTCGAAGTCGACCCTCTGTGACGGAGAATGACCGGACTTCCAGTGATCGACTAAGTAGAGGCAAACCCGACCGCGCGGAACCCCTAGGAG

      2010      2020      2030      2040      2050      2060      2070      2080      2090      2100
CTATCTCTCCTTCCCCAGTGCTGGGATAACAAGGTTGGCACCACATGAGCCTTTTAAAATGTGAGTTTGGAAGCTCAAACGCAGGTTTTCATGCTTGCAC
GATAGAGAGGAAGGGGTCACGACCCTATTGTTCCAACCGTGGTGTACTCGGAAAATTTTACACTCAAACCTTCGAGTTTGCGTCCAAAAGTACGAACGTG

      2110      2120      2130      2140      2150      2160      2170      2180      2190      2200
TGAAACTTCACAAGCTGAACCGTCTCCCTCTCCTTCCCTCTCTTTTTTCCTTTTCTTCTTCCTTTTTAAAACACATCTTGTCTTTAAAAAAAAAAAAAGG
ACTTTGAAGTGTTCGACTTGGCAGAGGGAGAGGAAGGGAGAGAAAAAAGGAAAAGAAGAAGGAAAAATTTTGTGTAGAACAGAAATTTTTTTTTTTTTCC
```

FIG. 5A

```
      2210       2220       2230       2240       2250       2260       2270       2280       2290       2300
CCCAAAACAAGTGTAAAGTATTTCCCTATGTGTGTGGAGGGAGGGAGTATAGGAGGCTGATTTCACTGAGATCCTGTTAAATTTGGGTGCCATAGCCAAT
GGGTTTTGTTCACATTTCATAAAGGGATACACACACCTCCCTCCCTCATATCCTCCGACTAAAGTGACTCTAGGACAATTTAAACCCACGGTATCGGTTA

      2310       2320       2330       2340       2350       2360       2370       2380       2390       2400
CAAAGACGCATCGTTTCCTCTAAGAATTCTAAATGGGGCGATTACCACGGGCCTGCAGGTTCTGGTTTGTATTAGAGGAGACACTGTCTTCTTAAGTAAA
GTTTCTGCGTAGCAAAGGAGATTCTTAAGATTTACCCCGCTAATGGTGCCCGGACGTCCAAGACCAAACATAATCTCCTCTGTGACAGAAGAATTCATTT

      2410       2420       2430       2440       2450       2460       2470       2480       2490       2500
ACATAGAAGGGGAAGTGTCCAGAATTGTAAATAAGGCTTCGAGAGAAGCCTTGTCTGGCCACCGGGATGGAGAAGACCTACCTTCGCCTATCCAGGATCC
TGTATCTTCCCCTTCACAGGTCTTAACATTTATTCCGAAGCTCTCTTCGGAACAGACCGGTGGCCCTACCTCTTCTGGATGGAAGCGGATAGGTCCTAGG

      2510       2520       2530       2540       2550       2560       2570       2580       2590       2600
ATCGTCCCTCCCTCTACCCAGATCTGACAGCCCTCCTTGGCTCTTTTGCTGAGGTTTGTTTGAGTTTGTTTTACTCTCTGCAAGAGAAGTTTCCTTAAAC
TAGCAGGGAGGGAGATGGGTCTAGACTGTCGGGAGGAACCGAGAAAACGACTCCAAACAAACTCAAACAAAATGAGAGACGTTCTCTTCAAAGGAATTTG

      2610       2620       2630       2640       2650       2660       2670       2680       2690       2700
ATTCTACCCTGTTCACAAGTAAATACACCTCTTAGCTAAGAGGCCACACACCCAGGGGAACACCGATAAAAAGAACAAGCCAGAACCTTCAGAACGCTGT
TAAGATGGGACAAGTGTTCATTTATGTGGAGAATCGATTCTCCGGTGTGTGGGTCCCCTTGTGGCTATTTTTCTTGTTCGGTCTTGGAAGTCTTGCGACA

      2710       2720       2730       2740       2750       2760       2770       2780       2790       2800
CGATAGGTACACCAAGCAGCCTTCATACGGAGTTTTCATTCGTGAGGAGCTGAATATACAACAAAGCTAAATGTGAGCAGACCAGGCATGCCTCTGCTAA
GCTATCCATGTGGTTCGTCGGAAGTATGCCTCAAAAGTAAGCACTCCTCGACTTATATGTTGTTTCGATTTACACTCGTCTGGTCCGTACGGAGACGATT

      2810       2820       2830       2840       2850       2860       2870       2880       2890       2900
ATGAGGATGCCCACACCAAACATGCCCAAGATCTTCAAGTATAATTTTATTATATAGATTCGCTATGTGTTGACATGTTTTTATAGTGAACCTGGATTTT
TACTCCTACGGGTGTGGTTTGTACGGGTTCTAGAAGTTCATATTAAAATAATATATCTAAGCGATACACAACTGTACAAAAATATCACTTGGACCTAAAA

      2910       2920       2930       2940       2950       2960       2970       2980       2990       3000
ACAAACCCTCCTGGTTTGCCACCTGCTTCTGGCACCATACTTGAGGCTTAGGCACGTGATAAAGGAGCATGCCTGTTTCCCCCCTTATTTTTTTTAAAGA
TGTTTGGGAGGACCAAACGGTGGACGAAGACCGTGGTATGAACTCCGAATCCGTGCACTATTTCCTCGTACGGACAAAGGGGGGAATAAAAAAAATTTCT

      3010       3020       3030       3040       3050       3060       3070       3080       3090       3100
AAAGCACCATGTTACATCATTAATCATGCATATCAGTGTAGTTTAGATCCGATGTAGAGACAATAATCTTATCTCTTTGTCTGGCTGAAAGACTGTCCTT
TTTCGTGGTACAATGTAGTAATTAGTACGTATAGTCACATCAAATCTAGGCTACATCTCTGTTATTAGAATAGAGAAACAGACCGACTTTCTGACAGGAA

      3110       3120       3130       3140       3150       3160       3170       3180       3190       3200
TAAACTATCATTCTAAATGCATTTGGTTTTTGCCAGGAGTAAAACATGTCACAAGATATTTGTTGTCATTTCCCAGGCGTGGAAGGAAAGGAATGGAAAG
ATTTGATAGTAAGATTTACGTAAACCAAAAACGGTCCTCATTTTGTACAGTGTTCTATAAACAACAGTAAAGGGTCCGCACCTTCCTTTCCTTACCTTTC

      3210       3220       3230       3240       3250       3260       3270       3280       3290       3300
AAAACGAGGGGTGAAGGCTGCTGTTCCTCTCTAGTCGCTACTTGAAGTCTACATAGCTGGGGGGGGGGGGGGGGACTGTTCACATGGGACCGGTTTCCTCT
TTTTGCTCCCCACTTCCGACGACAAGGAGAGATCAGCGATGAACTTCAGATGTATCGACCCCCCCCCCCCCCCTGACAAGTGTACCCTGGCCAAAGGAGA

      3310       3320       3330       3340       3350       3360       3370       3380       3390       3400
TTGTTCCTACACTGGCGCCTCTGGCAAGAAACTCTCCCTTCTCTTCCCCCCAAGCATATCTTGGCTGAAAGGTCAGCTCTGAAAAGGGGCCTGGCCAAAG
AACAAGGATGTGACCGCGGAGACCGTTCTTTGAGAGGGAAGAGAAGGGGGGTTCGTATAGAACCGACTTTCCAGTCGAGACTTTTCCCCGGACCGGTTTC

      3410       3420       3430       3440       3450       3460       3470       3480       3490       3500
TTACTGTAGGGGACCGTGGTCATGGAACTGGGTAGACAAAAGCACTCTAGCAGCCACTGGAGAAGGACCGGGGGCTCTTCTCTGTGCATTTGCCCTGGAG
AATGACATCCCCTGGCACCAGTACCTTGACCCATCTGTTTTCGTGAGATCGTCGGTGACCTCTTCCTGGCCCCCGAGAAGAGACACGTAAACGGGACCTC

      3510       3520       3530       3540       3550       3560       3570       3580       3590       3600
CCCTGACCACCGCCAGCTCCCTGCATCTCCTTGCTATGGGTTTTCTGGACCGAGCCAGGCAGGAGTTCACAACCGAAATGTCTTCTAGGGCTAATCAGGT
GGGACTGGTGGCGGTCGAGGGACGTAGAGGAACGATACCCAAAAGACCTGGCTCGGTCCGTCCTCAAGTGTTGGCTTTACAGAAGATCCCGATTAGTCCA

      3610       3620       3630       3640       3650       3660       3670       3680       3690       3700
AACTTCGGACGATTTAAAGTTGCCAGATGGACGAGAAAACAGTAGAGGCGTTGGCAACCTGGATAAGCGCCTATCTTCTAATTAAAACATTCAGACGGGG
TTGAAGCCTGCTAAATTTCAACGGTCTACCTGCTCTTTTGTCATCTCCGCAACCGTTGGACCTATTCGCGGATAGAAGATTAATTTTGTAAGTCTGCCCC

      3710       3720       3730       3740       3750       3760       3770       3780       3790       3800
CGGGGGATG-CGGTGGCCAAAGCACCATAAAACAAAACTTCCAAGTACTGACCAACTCACTGCAAGTTTGTGCCCCGAGTACATCTAGGTTCAGGGGTCT
GCCCCCTAC-GCCACCGGTTTCGTGGTATTTTGTTTTGAAGGTTCATGACTGGTTGAGTGACGTTCAAACACGGGGCTCATGTAGATCCAAGTCCCCAGA

      3810       3820       3830       3840       3850       3860       3870       3880       3890       3900
TGTCTTCATGCTCCCAACTGCGGGCGGATTTTTGGTCCCTTGGGACTTTCAGTGCAGCGGCGAAGAGAGTTCTGCACTTGCAGGCTCCTAATGAGGGCGC
ACAGAAGTACGAGGGTTGACGCCCGCCTAAAAACCAGGGAACCCTGAAAGTCACGTCGCCGCTTCTCTCAAGACGTGAACGTCCGAGGATTACTCCCGCG

      3910       3920       3930       3940       3950       3960       3970       3980       3990       4000
AGTGGGCCTCGTGTTTCTGGTGATGCTTCCCAGGTTGCTGGGGGCAGCAAGTGTCTCAGAGCCCATTACTGGCTACATTTTACTTCCACCAGAAACCGAG
TCACCCGGAGCACAAAGACCACTACGAAGGGTCCAACGACCCCCGTCGTTCACAGAGTCTCGGGTAATGACCGATGTAAAATGAAGGTGGTCTTTGGCTC

      4010       4020       4030       4040       4050       4060       4070       4080       4090       4100
CTGCGTCCAGATTTGCTCTCAGATGCGACTTGCCGCCCGGCACAGTTCCGGGGTAGTGGGGGAGTGGGCGTGGGAAACCGGGAAACCCAAACCTGGTATC
GACGCAGGTCTAAACGAGAGTCTACGCTGAACGGCGGGCCGTGTCAAGGCCCCATCACCCCCTCACCCGCACCCTTTGGCCCTTTGGGTTTGGACCATAG

      4110       4120       4130       4140       4150       4160       4170       4180       4190       4200
CAGTGGGGGGCGTGGCCGGACGCAGGGAGTCCCCACCCCTCCCGGTAATGACCCCGCCCCCATTCGCTAGTGTGTAGCCGGCGCTCTCTTTCTGCCCCTGA
GTCACCCCCCGCACCGGCCTGCGTCCCTCAGGGGTGGGGAGGGCCATTACTGGGGCGGGGGTAAGCGATCACACATCGGCCGCGAGAGAAAGACGGGACT

      4210       4220       4230       4240       4250       4260       4270       4280       4290       4300
GTCCTCAGGACCCCAAGAGAGTAAGCTGTGTTTCCTTAGATCGCGCGGACCGCTACCCGGCAGGACTGAAAGCCCAGACTGTGTCCCGCAGCCGGGATAA
CAGGAGTCCTGGGGTTCTCTCATTCGACACAAAGGAATCTAGCGCGCCTGGCGATGGGCCGTCCTGACTTTCGGGTCTGACACAGGGCGTCGGCCCTATT

      4310       4320       4330       4340       4350       4360       4370       4380       4390       4400
CCTGGCTGACCCGATTCCGCGGACACCGCTGCAGCCGCGGCTGGAGCCAGGGCGCCCGGTGCCCCGCGCTCTCCCCGGTCTTGCGCTGCGGGGGCGCATAC
GGACCGACTGGGCTAAGGCGCCTGTGGCGACGTCGGCGCCGACCTCGGTCCCGCGGCCACGGGGCGCGAGAGGGGCCAGAACGCGACGCCCCCGCGTATG
```

FIG. 5B

4410 4420 4430 4440 4450 4460 4470 4480

CGCCTCTGTGACTTCTTTGCGGGCCAGGGACGGAGAAGGAGTCTGTGCCTGAGAACTGGGCTCTGTGCCCAGCGCGAGGTGCAGATG
GCGGAGACACTGAAGAAACGCCCGGTCCCTGCCTCTTCCTCAGACACGGACTCTTGACCCGAGACACGGGTCGCGCTCCACGTCTAC

FIG.5C

VEGF	VEGFR2	Tie2
Screening primers	**Screening primers**	**Screening primers**
Primers: VF1-VR1A Product size: 0.69Kb	Primers: KF1-KR1 Product size: 0.45Kb	Primers: TF3-TR1 Product size: 0.45Kb
PCR program	**PCR program**	**PCR program**
Hot start	Hot start	Hot start
94°C 40 sec 65°C 1 min 30 sec 72°C 1 min 30 sec	94°C 40 sec 58°C 1 min 30 sec 72°C 1 min 30 sec	94°C 40 sec 58°C 1 min 30 sec 72°C 1 min 30 sec
40 cycles	40 cycles	40 cycles
Confirmation primers	**Confirmation primers**	**Confirmation primers**
Primers: VF2-VR2 Product size: 0.98Kb	Primers: KF2-KR2 Product size: 0.58Kb	Primers: TF2-TR1 Product size: 0.47Kb
PCR program	**PCR program**	**PCR program**
Hot start	Hot start	Hot start
94°C 40 sec 65°C 1 min 30 sec 72°C 1 min 30 sec	94°C 40 sec 65°C 1 min 30 sec 72°C 1 min 30 sec	94°C 40 sec 58°C 1 min 30 sec 72°C 1 min 30 sec
40 cycles	40 cycles	40 cycles

FIG. 6

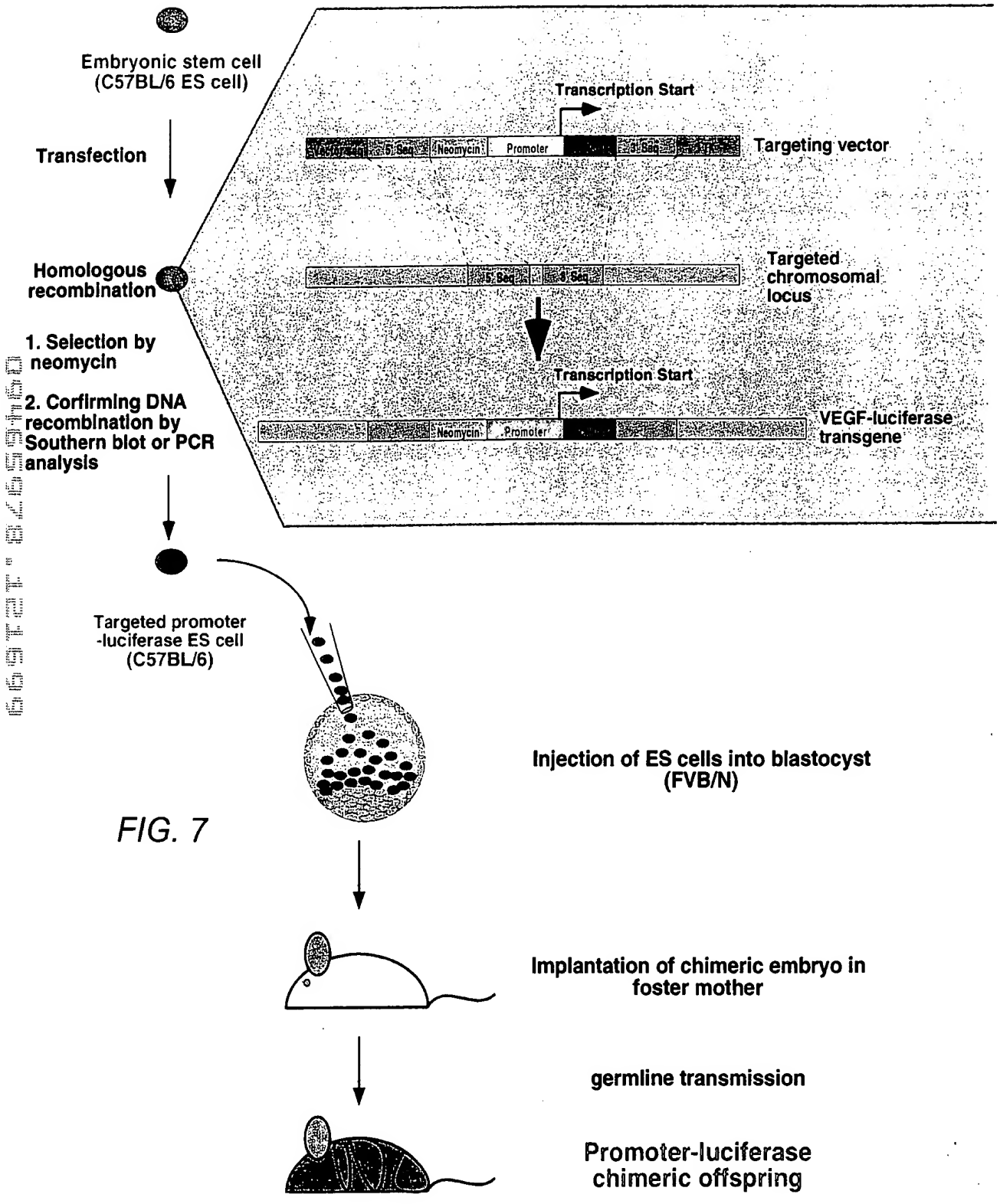
Embryonic stem cell
(C57BL/6 ES cell)
Transfection
Homologous recombination
1. Selection by neomycin
2. Corfirming DNA recombination by Southern blot or PCR analysis
Targeted promoter -luciferase ES cell (C57BL/6)
Transcription Start
Neomycin
Promoter
Targeting vector
Targeted chromosomal locus
Transcription Start
VEGF-luciferase transgene
Injection of ES cells into blastocyst (FVB/N)
Implantation of chimeric embryo in foster mother
germline transmission
Promoter-luciferase chimeric offspring

FIG. 7

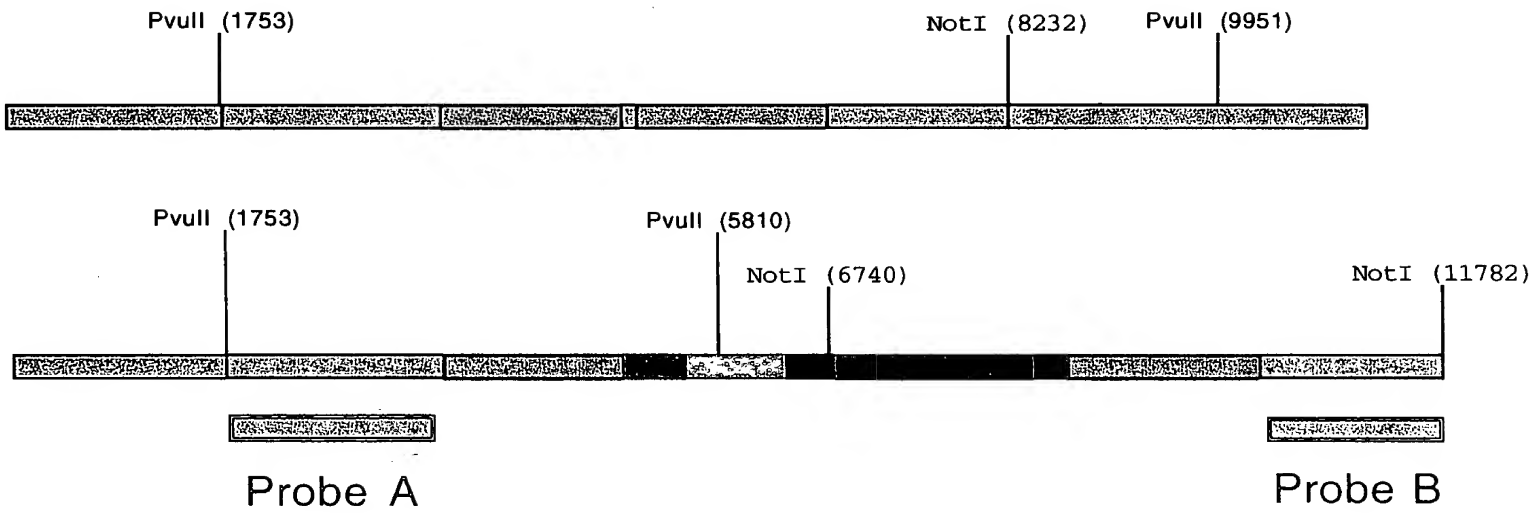

FIG. 8

Generation of Targeted Transgenic Mice

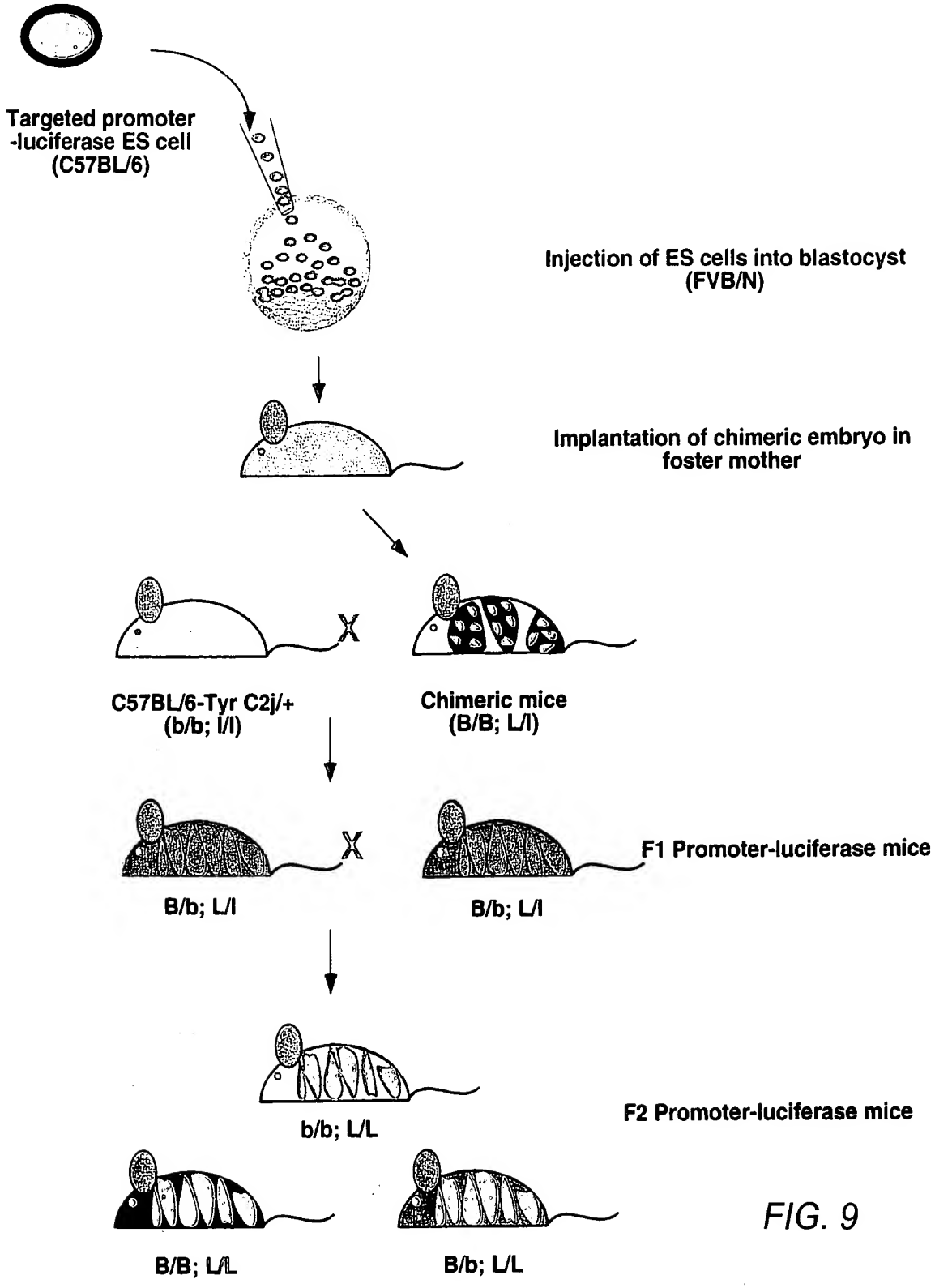

FIG. 9

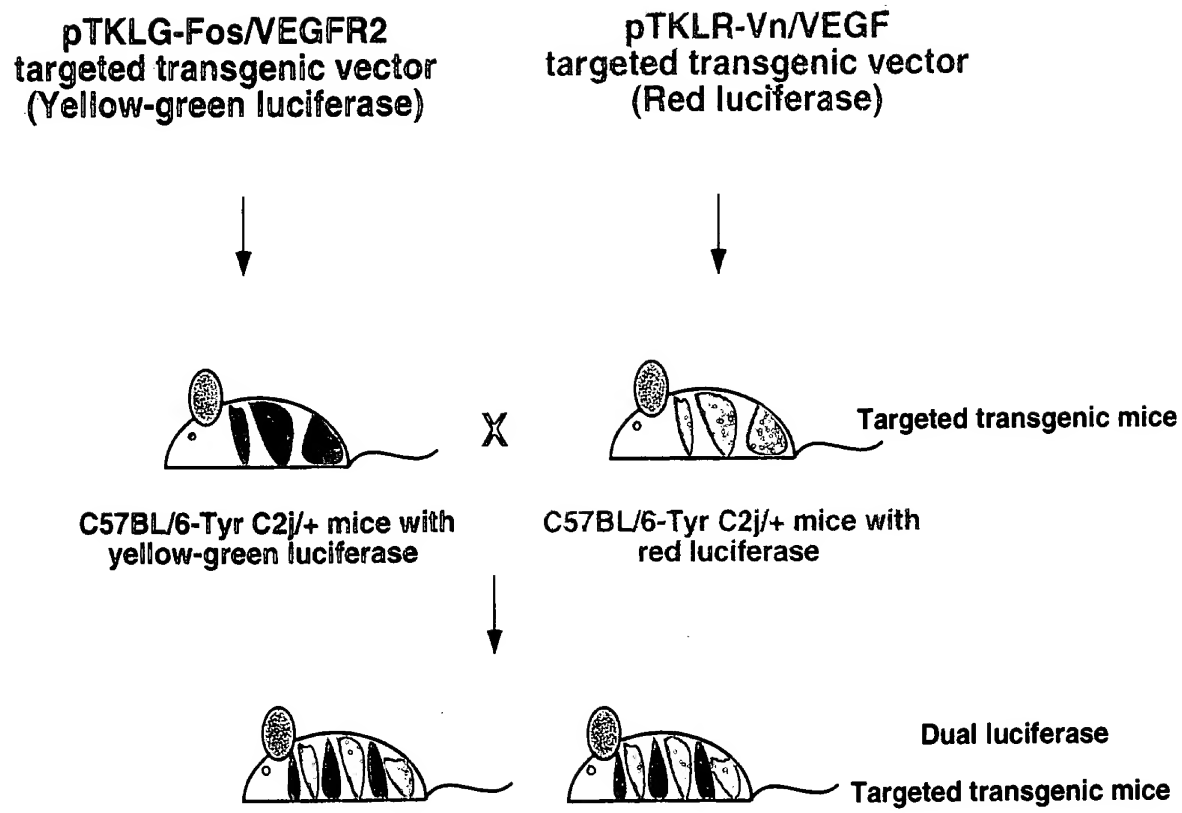
pTKLG-Fos/VEGFR2
targeted transgenic vector
(Yellow-green luciferase)
pTKLR-Vn/VEGF
targeted transgenic vector
(Red luciferase)
X
Targeted transgenic mice
C57BL/6-Tyr C2j/+ mice with
yellow-green luciferase
C57BL/6-Tyr C2j/+ mice with
red luciferase
Dual luciferase
Targeted transgenic mice

FIG. 10

10 20 30 40 50 60 70 80 90 100

AAATGTGCTGTCTTTAGAAGCCACTGCCTCAGCTTCTGCAGCTCAGATACCAAAGGAAGTCTGGTACACAGCATGATAAAAGACAATGGACGGGGTCAC
TTTACACGACAGAAATCTTCGGTGACGGAGTCGAAGACGTCGAGTCTATGGTTTCCTTCAGACCATGTGTCGTACTATTTTCTGTTACCCTGCCCCAGTG

110 120 130 140 150 160 170 180 190 200

AGTGGCTCCCGTCCCTTTCAGGGGTATGGAGACGAGCTGTAGAGAGATGTCTCCAGGGAGTTTTCATTAATCAGCAATTTAGTCAGATCTGTGCATCCTA
TCACCGAGGGCAGGGAAAGTCCCCATACCTCTGCTCGACATCTCTCTACAGAGGTCCCTCAAAAGTAATTAGTCGTTAAATCAGTCTAGACACGTAGGAT

210 220 230 240 250 260 270 280 290 300

TGCTTTACAAGAAATGTCAGTGGGCCTGAGATCATCAGATGGAGGTTCATCGGGTTTCAATGTCCCGTATCCTTTTGTAAGACCTTGAAGTTGGCAACGC
ACGAAATGTTCTTTACAGTCACCCGGACTCTAGTAGTCTACCTCCAAGTAGCCCAAAGTTACAGGGCATAGGAAAACATTCTGGAACTTCAACCGTTGCG

310 320 330 340 350 360 370 380 390 400

AGGAAAACAGGAACTCCACCCTGGTGCCGTGAATTGCAGAGCTGTTGTGTTGGTTTGTGACCATCTGCCCATTCTTCCTGTTATGACAGAGCTTGTGAAC
TCCTTTTGTCCTTGAGGTGGGACCACGGCACTTAACGTCTCGACAACACAACCAAACACTGGTAGACGGGTAAGAAGGACAATACTGTCTCGAACACTTG

410 420 430 440 450 460 470 480 490 500

TTTAACTGGGACTGGGGCAAAGTCAATCCCACCTTTATACAATGAATTGCTGAAGAGGCCTTTTAAAACTTGGAGTGTGCATTGTTTATGGAAGGGCTTT
AAATTGACCCTGACCCCGTTTCAGTTAGGGTGGAAATATGTTACTTAACGACTTCTCCGGAAAATTTTGAACCTCACACGTAACAAATACCTTCCCGAAA

510

CCTATTGGATC
GGATAACCTAG

FIG. 11

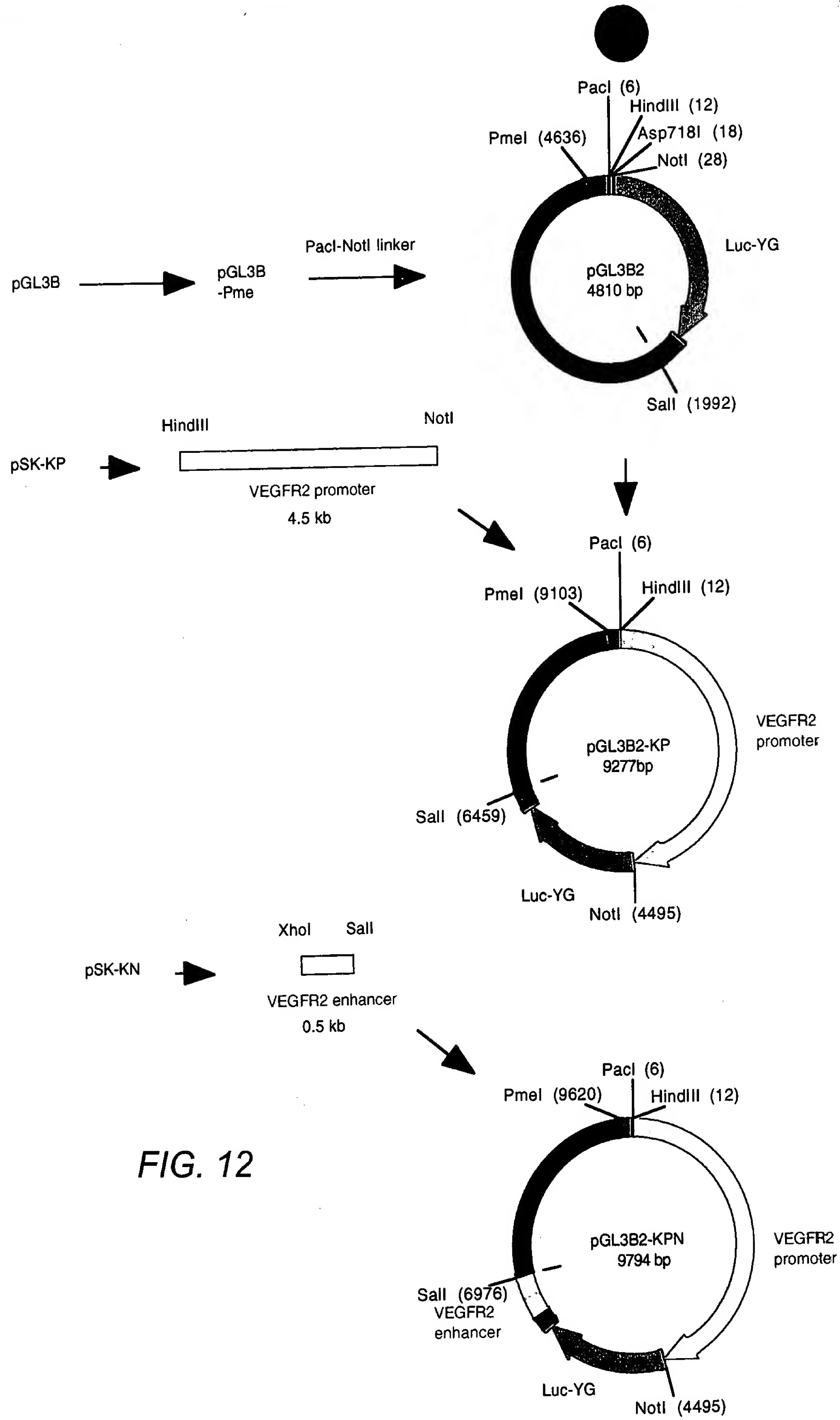
PacI (6)
HindIII (12)
Asp718I (18)
NotI (28)
PmeI (4636)
PacI-NotI linker
pGL3B
pGL3B
-Pme
pGL3B2
4810 bp
Luc-YG
SalI (1992)
HindIII
NotI
pSK-KP
VEGFR2 promoter
4.5 kb
PacI (6)
PmeI (9103)
HindIII (12)
pGL3B2-KP
9277bp
VEGFR2
promoter
SalI (6459)
Luc-YG
NotI (4495)
XhoI
SalI
pSK-KN
VEGFR2 enhancer
0.5 kb
PacI (6)
PmeI (9620)
HindIII (12)
pGL3B2-KPN
9794 bp
VEGFR2
promoter
SalI (6976)
VEGFR2
enhancer
Luc-YG
NotI (4495)

FIG. 12

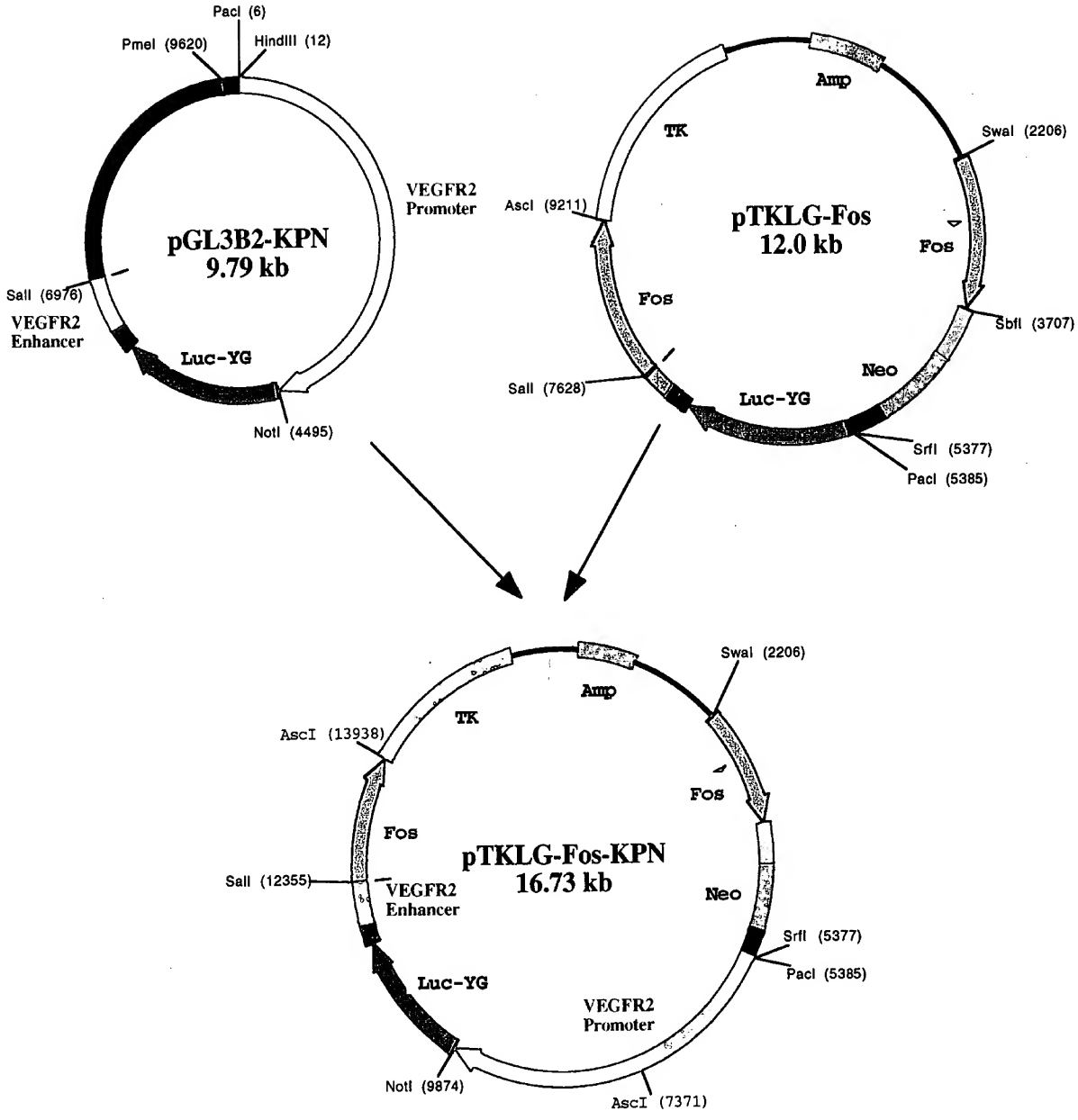
PacI (6)
PmeI (9620)
HindIII (12)
pGL3B2-KPN
9.79 kb
VEGFR2
Promoter
SalI (6976)
VEGFR2
Enhancer
Luc-YG
NotI (4495)
Amp
TK
SwaI (2206)
AscI (9211)
pTKLG-Fos
12.0 kb
Fos
Fos
SbfI (3707)
Neo
SalI (7628)
Luc-YG
SrfI (5377)
PacI (5385)
SwaI (2206)
Amp
TK
AscI (13938)
Fos
Fos
pTKLG-Fos-KPN
16.73 kb
SalI (12355)
VEGFR2
Enhancer
Neo
SrfI (5377)
PacI (5385)
Luc-YG
VEGFR2
Promoter
NotI (9874)
AscI (7371)

FIG. 13

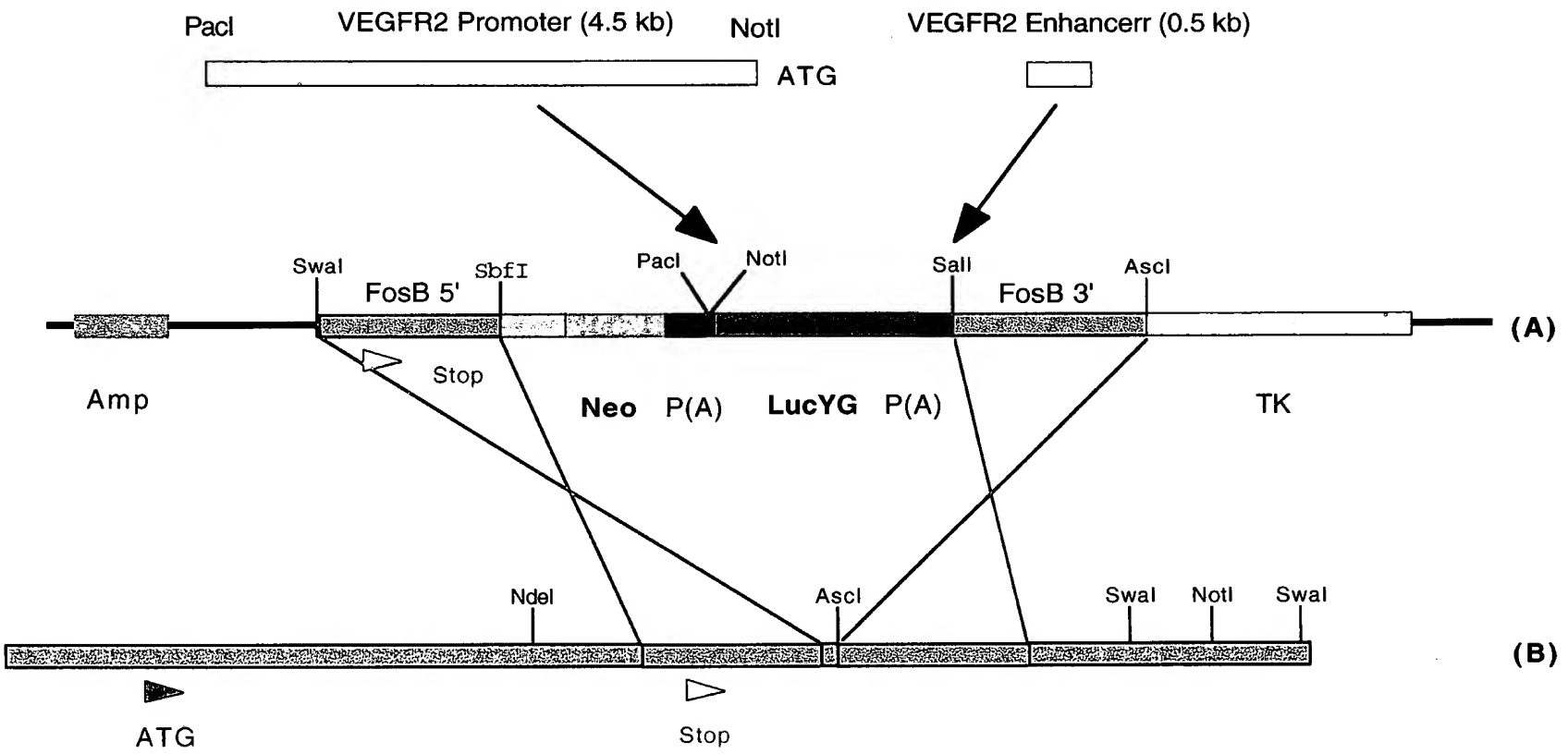

FIG. 14

[redacted]

```
       10        20        30        40        50        60        70        80        90       100
GGTACCAAAGCATAGAACTACAGATCCGCTCTCTGCCTGTACCACCCTCTGGCATTTAATCACACAATGCTTGGTTTTGTTCTTCAACTTTTCCTGTTAT
CCATGGTTTCGTATCTTGATGTCTAGGCGAGAGACGGACATGGTGGGAGACCGTAAATTAGTGTGTTACGAACCAAAACAAGAAGTTGAAAAGGACAATA

      110       120       130       140       150       160       170       180       190       200
GATGCAGTCCCTGGCTTGTGTAACTATGAGCTTCAAAAGCAAAGAACGCATCATCTATTTTTGTGTCTCTTCTTCCAAGGACTTAGTGTATCACTTACTG
CTACGTCAGGGACCGAACACATTGATACTCGAAGTTTTCGTTTCTTGCGTAGTAGATAAAAACACAGAGAAGAAGGTTCCTGAATCACATAGTGAATGAC

      210       220       230       240       250       260       270       280       290       300
GCTAAATGCTTGAGACAAAAACAGGGATTAATGAAGAAGAAAGAGAAAGAAAAGGAAGGGAAAGTGCCCACAATTACTGACAGGGTTTCAGTAAAGCAGT
CGATTTACGAACTCTGTTTTTGTCCCTAATTACTTCTTCTTTCTCTTTCTTTTCCTTCCCTTTCACGGGTGTTAATGACTGTCCCAAAGTCATTTCGTCA

      310       320       330       340       350       360       370       380       390       400
CTAGAGGGTCAGGTATTTTCCATAGCCATGCCCCAGAGTGGGTGTTGCCACTTTAGCTGCCCTGGTCTGGCTGAAGGCCAGGACTTGATTGTTGATGGCC
GATCTCCCAGTCCATAAAAGGTATCGGTACGGGGTCTCACCCACAACGGTGAAATCGACGGGACCAGACCGACTTCCGGTCCTGAACTAACAACTACCGG

      410       420       430       440       450       460       470       480       490       500
CTTCCTTTGCTGCTAGTCACTGTTAAGTACTGCAGATTTACAGAAAGCTTCATGGAGGTCTGTAAGAAGCCAGAGGTGATAACACCAAGATTTAGAGCCA
GAAGGAAACGACGATCAGTGACAATTCATGACGTCTAAATGTCTTTCGAAGTACCTCCAGACATTCTTCGGTCTCCACTATTGTGGTTCTAAATCTCGGT

      510       520       530       540       550       560       570       580       590       600
CTGACCAGCAGAATGCAGAATGTCCAGGCTATGATCCAGGTTGTAGATCCTGATCTGACTACTCAAGACTGGTTGAAGGCAAGGTTCACTTGGATTCACT
GACTGGTCGTCTTACGTCTTACAGGTCCGATACTAGGTCCAACATCTAGGACTAGACTGATGAGTTCTGACCAACTTCCGTTCCAAGTGAACCTAAGTGA

      610       620       630       640       650       660       670       680       690       700
CTATTTGCCAGCAGATGTTTTAAATCCATCATATATATATATATATCTCCATTACTTTAGGACAGTGGTTCTCAGCCTTCCTAATGCTGTAGCCCTTTAA
GATAAACGGTCGTCTACAAAATTTAGGTAGTATATATATATATATAGAGGTAATGAAATCCTGTCACCAAGAGTCGGAAGGATTACGACATCGGGAAATT

      710       720       730       740       750       760       770       780       790       800
TAGAGTTCCTCATATTGTGATTGTAAAAATTATTTGTTGCTACTTCATGACTAATTTTGCTACTGTGAAAGGGTCATTTTACCCCAGGCTGTTGAGACC
ATCTCAAGGAGTATAACACTAACATTTTTAATAAAACAACGATGAAGTACTGATTAAAACGATGACACTTTCCCAGTAAAATGGGGTCCGACAACTCTGG

      810       820       830       840       850       860       870       880       890       900
CACATGTTGGGAACCACTACTTTAGAAGGCATTGGGGTTGGAGAAGAACATGAAGAATAGAGTAACAGTGGTCAGTTTTGGTTCATTATATCACAGAAAC
GTGTACAACCCTTGGTGATGAAATCTTCCGTAACCCCAACCTCTTCTTGTACTTCTTATCTCATTGTCACCAGTCAAAACCAAGTAATATAGTGTCTTTG

      910       920       930       940       950       960       970       980       990      1000
ATTCACTTTAAGGTTTCAGCATGTTTGTTGTGTATATGTGATTGTGTAAAGACTTCACCAGGTCTTTCTTTAATCACCATACCTAACATCTTCACCACTC
TAAGTGAAATTCCAAAGTCGTACAAACAACACATATACACTAACACATTTCTGAAGTGGTCCAGAAAGAAATTAGTGGTATGGATTGTAGAAGTGGTGAG

     1010      1020      1030      1040      1050      1060      1070      1080      1090      1100
CATATCCATCAGCTTCACCTTGTACTCTAGCATTTGGGCATTCATCCTGTACCAGGGCAGGCATCCATTCTTTTGCAACTCACATTGTTTCCTAGTTTTG
GTATAGGTAGTCGAAGTGGAACATGAGATCGTAAACCCGTAAGTAGGACATGGTCCCGTCCGTAGGTAAGAAAACGTTGAGTGTAACAAAGGATCAAAAC

     1110      1120      1130      1140      1150      1160      1170      1180      1190      1200
ATTATTACCAACAATGCTTCTAGACCATGAATTTTGGTCTTTGACTTTTGCTTGGTAAACATCATAAAACAATCCAGTGGTGGTGGTGGTGCCGCTGCTG
TAATAATGGTTGTTACGAAGATCTGGTACTTAAAACCAGAAACTGAAAACGAACCATTTGTAGTATTTTGTTAGGTCACCACCACCACCACGGCGACGAC

     1210      1220      1230      1240      1250      1260      1270      1280      1290      1300
CTGGTGGTGGTGGTAAAGCAGGAAGCCATAAAGTGCCTTTATTCAATCTGTATTTGATACAAATTGTTATTTCTTCCCATGTAAAAGATATGGCATCTGA
GACCACCACCACCATTTCGTCCTTCGGTATTTCACGGAAATAAGTTAGACATAAACTATGTTTAACAATAAAGAAGGGTACATTTTCTATACCGTAGACT

     1310      1320      1330      1340      1350      1360      1370      1380      1390      1400
AGTGTAGAGGTCTGAATTCAAACCTCACATCACCAGATAGTATATTACAGACTCAACAAATAATACACGGCTTTGCCTGACTTCAAAGCCCTGTTCTTGA
TCACATCTCCAGACTTAAGTTTGGAGTGTAGTGGTCTATCATATAATGTCTGAGTTGTTTATTATGTGCCGAAACGGACTGAAGTTTCGGGACAAGAACT

     1410      1420      1430      1440      1450      1460      1470      1480      1490      1500
CGTAAGTATATGAGTAACAATGGTAGCACCTTAGTTTTTATCAGTTCACTAAATATTTATATAAGACCTACTATGAAGGGAGATAGAAGGGTATGAGGTG
GCATTCATATACTCATTGTTACCATCGTGGAATCAAAAATAGTCAAGTGATTTATAAATATATTCTGGATGATACTTCCCTCTATCTTCCCATACTCCAC

     1510      1520      1530      1540      1550      1560      1570      1580      1590      1600
GGGTCATGGGAATAGGAAAACGGTGGAAGGGAGAAGGAGAATTAACAAAAGCTAATTATGTTTGAAAATGCCACAATGAAACCTAATTTACAAAAGAACC
CCCAGTACCCTTATCCTTTTGCCACCTTCCCTCTTCCTCTTAATTGTTTTCGATTAATACAAACTTTTACGGTGTTACTTTGGATTAAATGTTTTCTTGG

     1610      1620      1630      1640      1650      1660      1670      1680      1690      1700
ACTATATGACCTTCACAGTGTGTGCTAAGTCTTGGAGATTTAGTGGTGAAGAAGTCAGGTGTGTTTCCAATCTCATGGAGGATGTAATCAGTTAGAGAGC
TGATATACTGGAAGTGTCACACACGATTCAGAACCTCTAAATCACCACTTCTTCAGTCCACACAAAGGTTAGAGTACCTCCTACATTAGTCAATCTCTCG

     1710      1720      1730      1740      1750      1760      1770      1780      1790      1800
ACAGGAGCACATAAAAAGATAGGCAAAAATGTATGATTAGTACCATGTAAGATATGAAGGGGAACACAGGAAACTAGTGGGGAGACCTAATTTAGTTTGA
TGTCCTCGTGTATTTTTCTATCCGTTTTTACATACTAATCATGGTACATTCTATACTTCCCCTTGTGTCCTTTGATCACCCCTCTGGATTAAATCAAACT

     1810      1820      1830      1840      1850      1860      1870      1880      1890      1900
GTGGTCTTCAAAGACCCTTTAGAAGCTGAGAACTAAAGACAGCAAGCAAGGTGAGGGCAGCATCTCCACCTTTCCAGTGGAATGAGCAACTTAGGGTATA
CACCAGAAGTTTCTGGGAAATCTTCGACTCTTGATTTCTGTCGTTCGTTCCACTCCCGTCGTAGAGGTGGAAAGGTCACCTTACTCGTTGAATCCCATAT

     1910      1920      1930      1940      1950      1960      1970      1980      1990      2000
CAGCTGATTCCCACATTGTCAACAAGGCTCTTCAGAGACTAGAGATGCACTAATGATGACCATACCCAGCTTTTAAGGAAGGTTTCTGAGCATGTCCAAG
GTCGACTAAGGGTGTAACAGTTGTTCCGAGAAGTCTCTGATCTCTACGTGATTACTACTGGTATGGGTCGAAAATTCCTTCCAAAGACTCGTACAGGTTC

     2010      2020      2030      2040      2050      2060      2070      2080      2090      2100
CACCCTACACTAGGCATTGGAAATCAACATGTCCAGAGATGGAAGTGACAGTCAGTAAGCCAACCCTTTTCAAAACTTCCAAAGCTATTACTCGTCAACT
GTGGGATGTGATCCGTAACCTTTAGTTGTACAGGTCTCTACCTTCACTGTCAGTCATTCGGTTGGGAAAAGTTTTGAAGGTTTCGATAATGAGCAGTTGA

     2110      2120      2130      2140      2150      2160      2170      2180      2190      2200
CTCCAGACATATGGGCCCCGAGTGTGTTGGGAAGCTCTCATTATTGTTCTTTGATTGGTTCTCTACATTCCGAGATCCAAGGAGCAGTTATCTCAGGTAG
GAGGTCTGTATACCCGGGGCTCACACAACCCTTCGAGAGTAATAACAAGAAACTAACCAAGAGATGTAAGGCTCTAGGTTCCTCGTCAATAGAGTCCATC
```

FIG. 15-1

09455798 . 121600

[redacted]

2210 2220 2230 2240 2250 2260 2270 2280 2290 2300
AGGATCGTGGAATGTCTGCCCATGATTAACTTCAATTTATACCTGTAAGTTATACCACATCCTAAACACGCTGATGTCCCAGAGAACATTTTGACCAGCT
TCCTAGCACCTTACAGACGGGTACTAATTGAAGTTAAATATGGACATTCAATATGGTGTAGGATTTGTGCGACTACAGGGTCTCTTGTAAAACTGGTCGA

2310 2320 2330 2340 2350 2360 2370 2380 2390 2400
GCTAACAAAACCCAGGAGCATTTAGAAAAAAACTGAGTCACCCACCGTTCTGGATAATGATGGAGAGAAACAAATGGGATTATTCTTACAGAGTATGAAA
CGATTGTTTTGGGTCCTCGTAAATCTTTTTTTGACTCAGTGGGTGGCAAGACCTATTACTACCTCTCTTTGTTTACCCTAATAAGAATGTCTCATACTTT

2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
GTTACATAATTTTCCTGGATAATGGAGAATTAATTAAACATCAGCATCTTTTCTGGACTGCAGAGGGAAGACAGAGGTGAAGCCAATCTTTCCGGGAAAT
CAATGTATTAAAAGGACCTATTACCTCTTAATTAATTTGTAGTCGTAGAAAAGACCTGACGTCTCCCTTCTGTCTCCACTTCGGTTAGAAAGGCCCTTTA

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600
GGAGGAGGAAAGAATTTGACTACTATTTGGGGGTTAACAATACATCTTACTAGCATGGCAAAGGAAACTGGGCTGCTTTTCAGAGTAAGCCACCCCAGTA
CCTCCTCCTTTCTTAAACTGATGATAAACCCCCAATTGTTATGTAGAATGATCGTACCGTTTCCTTTGACCCGACGAAAAGTCTCATTCGGTGGGGTCAT

2610 2620 2630 2640 2650 2660 2670 2680 2690 2700
GATGCTGCAAGGCTGTGCTTTCATCCCAGGAGAAAGTCAACAGGGCCAGGCATGCCAGAACATGCCCATAATGTAACCACTTAGGCTGAGGCAGAAAGAT
CTACGACGTTCCGACACGAAAGTAGGGTCCTCTTTCAGTTGTCCCGGTCCGTACGGTCTTGTACGGGTATTACATTGGTGAATCCGACTCCGTCTTTCTA

2710 2720 2730 2740 2750 2760 2770 2780 2790 2800
CAAAAATCCCAGGCCAGCTTAGTTTGTGTAACAAGACCTTTGCTCAAACAAAGATTTACAAAACAAACAAGCAAACAAACAAATATAAAAAAGGAGAAGA
GTTTTTAGGGTCCGGTCGAATCAAACACATTGTTCTGGAAACGAGTTTGTTTCTAAATGTTTTGTTTGTTCGTTTGTTTGTTTATATTTTTTCCTCTTCT

2810 2820 2830 2840 2850 2860 2870 2880 2890 2900
AAATAACTGCCAGGGGAGGCTGTGAGCAATGAAGACTTGATGAGTGACCATCTCGCACAGTGGACGCTTGTGTCTAGAAGGTAAGGGCTTGGCAATGTTT
TTTATTGACGGTCCCCTCCGACACTCGTTACTTCTGAACTACTCACTGGTAGAGCGTGTCACCTGCGAACACAGATCTTCCATTCCCGAACCGTTACAAA

2910 2920 2930 2940 2950 2960 2970 2980 2990 3000
CCCAGGTTTTCCATTCCTGGTTTATATGGCTTGAGGCCAGTGGACTTCACAATGTCTCAGCTTCCAGGTCTTTATACAGAGCATATTAGCCACATGTGGT
GGGTCCAAAAGGTAAGGACCAAATATACCGAACTCCGGTCACCTGAAGTGTTACAGAGTCGAAGGTCCAGAAATATGTCTCGTATAATCGGTGTACACCA

3010 3020 3030 3040 3050 3060 3070 3080 3090 3100
AGCTTGTGCCTGTAATGCTGGCACTTGAGAGACCAAGACAGGAGGATTGCCACAAGTCTCCATCCAGCCTAGGTGCTGTGTCACTCTGTCTCACCCCTGA
TCGAACACGGACATTACGACCGTGAACTCTCTGGTTCTGTCCTCCTAACGGTGTTCAGAGGTAGGTCGGATCCACGACACAGTGAGACAGAGTGGGGACT

3110 3120 3130 3140 3150 3160 3170 3180 3190 3200
CCCAGTCCCACCCAACATCAAACAGGCTATCACTGTGACACTGGTACTGAGTCAGAATCACCCAGATTAAAGATTCTGGGAGATCAGTCCTGGGGATGCG
GGGTCAGGGTGGGTTGTAGTTTGTCCGATAGTGACACTGTGACCATGACTCAGTCTTAGTGGGTCTAATTTCTAAGACCCTCTAGTCAGGACCCCTACGC

3210 3220 3230 3240 3250 3260 3270 3280 3290 3300
GGAAGTGAGACCAGTTATTTAATAATTCTTATACTCATGAGATGATGGATCCAGATGAGAAATTGTAAAAATTTTAGGTTTTATAATTGAAGAAATAGGT
CCTTCACTCTGGTCAATAAATTATTAAGAATATGAGTACTCTACTACCTAGGTCTACTCTTTAACATTTTTAAAATCCAAAATATTAACTTCTTTATCCA

3310 3320 3330 3340 3350 3360 3370 3380 3390 3400
GGTTTCTTCAGGTTACATCTCTCCACTGTTGGTCATTTCAGCTAAGGTCACTCCCCATTGATTCCTGTGAGGCTCTCACATCCCAGGTCTCTGGGACTTT
CCAAAGAAGTCCAATGTAGAGAGGTGACAACCAGTAAAGTCGATTCCAGTGAGGGGTAACTAAGGACACTCCGAGAGTGTAGGGTCCAGAGACCCTGAAA

3410 3420 3430 3440 3450 3460 3470 3480 3490 3500
CTAGAGGTTCCCGCTGCTTCCCAGCCCTGAAAATGCGTATTTCTATTCATTCTCCTGGCATTCTGGGCTTCTCTCCTGTCCCCCGCCCCACCCAACACCT
GATCTCCAAGGGCGACGAAGGGTCGGGACTTTTACGCATAAAGATAAGTAAGAGGACCGTAAGACCCGAAGAGAGGACAGGGGGCGGGGTGGGTTGTGGA

3510 3520 3530 3540 3550 3560 3570 3580 3590 3600
GATCCTGCCCCCTTTCTCTCCCCCTTCTCTCTCTAAACCAGGTCCCTCCCTCCCTCTGCTTCCCATGATTATTTTGTTCCCTCCTCTAAATGAGTCTGAA
CTAGGACGGGGGAAAGAGAGGGGGAAGAGAGAGATTTGGTCCAGGGAGGGAGGGAGACGAAGGGTACTAATAAAACAAGGGAGGAGATTTACTCAGACTT

3610 3620 3630 3640 3650 3660 3670 3680 3690 3700
GCATCCTCACTTGGACNTTCCTTCTTGTTAAACTTCATATGGTCTGTGAGTTGTATCATGGGTATTCTGTACTTTTTTGGCTAATGTTTCACTTATCAGT
CGTAGGAGTGAACCTGNAAGGAAGAACAATTTGAAGTATACCAGACACTCAACATAGTACCCATAAGACATGAAAAAACCGATTACAAAGTGAATAGTCA

3710 3720 3730 3740 3750 3760 3770 3780 3790 3800
GAGTGCAAACCAGGCATATCCTTTTGAGTTTGGGTTACCTCACTCAGGATGATATTTTCTAGTTCTATCCATTCGCCTGCAAAATTCATGATGTCCTAAT
CTCACGTTTGGTCCGTATAGGAAAACTCAAACCCAATGGAGTGAGTCCTACTATAAAAGATCAAGATAGGTAAGCGGACGTTTTAAGTACTACAGGATTA

3810 3820 3830 3840 3850 3860 3870 3880 3890 3900
TTTTAGTAGCTGAATAGTATTCCATTGTGTAAATGAACCATATTTTCTGCATCTGTTCTTCAGCTGAGGGAAATCTGGGTTGTTTCCAGCTTCTAGGTAT
AAAATCATCGACTTATCATAAGGTAACACATTTACTTGGTATAAAAGACGTAGACAAGAAGTCGACTCCCTTTAGACCCAACAAAGGTCGAAGATCCATA

3910 3920 3930 3940 3950 3960 3970 3980 3990 4000
TATAAATAAGGTTGCTATGAACATAGTGGAACACATATCCTTGAGGTATGGTAGAGCATCTTTTGGGTATATATCCAGGAGTGGATAGTTGGGTTTTCAG
ATATTTATTCCAACGATACTTGTATCACCTTGTGTATAGGAACTCCATACCATCTCGTAGAAAACCCATATATAGGTCCTCACCTATCAACCCAAAAGTC

4010 4020 4030 4040 4050 4060 4070 4080 4090 4100
GTAGAACTATTTCCAATTTTCTAAGGAACCACCAGATTGATTTTTAGATAGACAGGGCCCCTAGTGGAGAGATGGGGCCAAACACCTACCTTCAAAAATT
CATCTTGATAAAGGTTAAAAGATTCCTTGGTGGTCTAACTAAAAATCTATCTGTCCCGGGGATCACCTCTCTACCCCGGTTTGTGGATGGAAGTTTTTAA

4110 4120 4130 4140 4150 4160 4170 4180 4190 4200
TGGTCCAGAATTGTTCCTCTCTAAAAGAAATGCAGGGACAAAAATGAAACAGAGACTGACCAACCCAACTTAGGATCCATCCTATGGGCAAGCACCAAAC
ACCAGGTCTTAACAAGGAGAGATTTTCTTTACGTCCCTGTTTTTACTTTGTCTCTGACTGGTTGGGTTGAATCCTAGGTAGGATACCCGTTCGTGGTTTG

4210 4220 4230 4240 4250 4260 4270 4280 4290 4300
CCAGACTCTATTATTGATGCCATGTTGTGCTTGCAGACAGGAGCTTAGCATGGCTGTCCTCTGAGACACTCTATCAGCAGCTGACTGGGACAGATGCAGA
GGTCTGAGATAATAACTACGGTACAACACGAACGTCTGTCCTCGAATCGTACCGACAGGAGACTCTGTGAGATAGTCGTCGACTGACCCTGTCTACGTCT

FIG. 15-2

4310 4320 4330 4340 4350 4360 4370 4380 4390 4400
TGCCAACCCTTGAACTGAGGTCCAGGACCCCTATGGAAGAATTAGGGGAAGGTTTGAAGGAGCTGAAGGGGATGGCAACCCCATAGGAAAAACAAGTGTC
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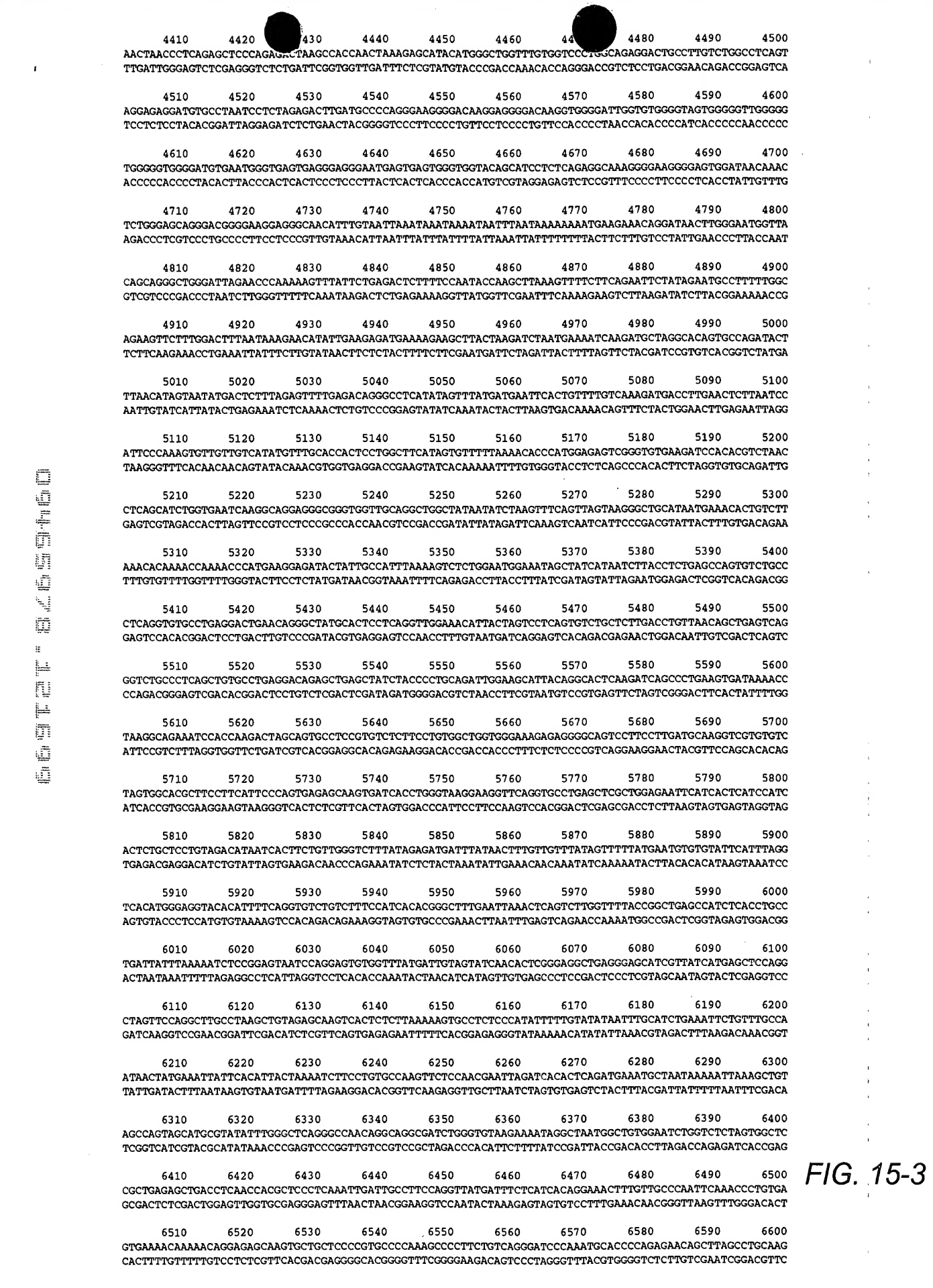
4410 4420 4430 4440 4450 4460 4470 4480 4490 4500
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TTGATTGGGAGTCTCGAGGGTCTCTGATTCGGTGGTTGATTTCTCGTATGTACCCGACCAAACACCAGGGACCGTCTCCTGACGGAACAGACCGGAGTCA
4510 4520 4530 4540 4550 4560 4570 4580 4590 4600
AGGAGAGGATGTGCCTAATCCTCTAGAGACTTGATGCCCCAGGGAAGGGGACAAGGAGGGGACAAGGTGGGGATTGGTGTGGGGTAGTGGGGGTTGGGGG
TCCTCTCCTACACGGATTAGGAGATCTCTGAACTACGGGGTCCCTTCCCCTGTTCCTCCCCTGTTCCACCCCTAACCACACCCCATCACCCCCAACCCCC
4610 4620 4630 4640 4650 4660 4670 4680 4690 4700
TGGGGGTGGGGATGTGAATGGGTGAGTGAGGGAGGGAATGAGTGAGTGGGTGGTACAGCATCCTCTCAGAGGCAAAGGGGAAGGGGAGTGGATAACAAAC
ACCCCCACCCCTACACTTACCCACTCACTCCCTCCCTTACTCACTCACCCACCATGTCGTAGGAGAGTCTCCGTTTCCCCTTCCCCTCACCTATTGTTTG
4710 4720 4730 4740 4750 4760 4770 4780 4790 4800
TCTGGGAGCAGGGACGGGGAAGGAGGGCAACATTTGTAATTAAATAAATAAAATAATTTAATAAAAAAAATGAAGAAACAGGATAACTTGGGAATGGTTA
AGACCCTCGTCCCTGCCCCTTCCTCCCGTTGTAAACATTAATTTATTTATTTTATTAAATTATTTTTTTTACTTCTTTGTCCTATTGAACCCTTACCAAT
4810 4820 4830 4840 4850 4860 4870 4880 4890 4900
CAGCAGGGCTGGGATTAGAACCCAAAAAGTTTATTCTGAGACTCTTTTCCAATACCAAGCTTAAAGTTTTCTTCAGAATTCTATAGAATGCCTTTTTGGC
GTCGTCCCGACCCTAATCTTGGGTTTTTCAAATAAGACTCTGAGAAAAGGTTATGGTTCGAATTTCAAAAGAAGTCTTAAGATATCTTACGGAAAAACCG
4910 4920 4930 4940 4950 4960 4970 4980 4990 5000
AGAAGTTCTTTGGACTTTAATAAAGAACATATTGAAGAGATGAAAAGAAGCTTACTAAGATCTAATGAAAATCAAGATGCTAGGCACAGTGCCAGATACT
TCTTCAAGAAACCTGAAATTATTTCTTGTATAACTTCTCTACTTTTCTTCGAATGATTCTAGATTACTTTTAGTTCTACGATCCGTGTCACGGTCTATGA
5010 5020 5030 5040 5050 5060 5070 5080 5090 5100
TTAACATAGTAATATGACTCTTTAGAGTTTTGAGACAGGGCCTCATATAGTTTATGATGAATTCACTGTTTTGTCAAAGATGACCTTGAACTCTTAATCC
AATTGTATCATTATACTGAGAAATCTCAAAACTCTGTCCCGGAGTATATCAAATACTACTTAAGTGACAAAACAGTTTCTACTGGAACTTGAGAATTAGG
5110 5120 5130 5140 5150 5160 5170 5180 5190 5200
ATTCCCAAAGTGTTGTTGTCATATGTTTGCACCACTCCTGGCTTCATAGTGTTTTTAAAACACCCATGGAGAGTCGGGTGTGAAGATCCACACGTCTAAC
TAAGGGTTTCACAACAACAGTATACAAACGTGGTGAGGACCGAAGTATCACAAAAATTTTGTGGGTACCTCTCAGCCCACACTTCTAGGTGTGCAGATTG
5210 5220 5230 5240 5250 5260 5270 5280 5290 5300
CTCAGCATCTGGTGAATCAAGGCAGGAGGGCGGGTGGTTGCAGGCTGGCTATAATATCTAAGTTTCAGTTAGTAAGGGCTGCATAATGAAACACTGTCTT
GAGTCGTAGACCACTTAGTTCCGTCCTCCCGCCCACCAACGTCCGACCGATATTATAGATTCAAAGTCAATCATTCCCGACGTATTACTTTGTGACAGAA
5310 5320 5330 5340 5350 5360 5370 5380 5390 5400
AAACACAAAACCAAAACCCATGAAGGAGATACTATTGCCATTTAAAAGTCTCTGGAATGGAAATAGCTATCATAATCTTACCTCTGAGCCAGTGTCTGCC
TTTGTGTTTTGGTTTTGGGTACTTCCTCTATGATAACGGTAAATTTTCAGAGACCTTACCTTTATCGATAGTATTAGAATGGAGACTCGGTCACAGACGG
5410 5420 5430 5440 5450 5460 5470 5480 5490 5500
CTCAGGTGTGCCTGAGGACTGAACAGGGCTATGCACTCCTCAGGTTGGAAACATTACTAGTCCTCAGTGTCTGCTCTTGACCTGTTAACAGCTGAGTCAG
GAGTCCACACGGACTCCTGACTTGTCCCGATACGTGAGGAGTCCAACCTTTGTAATGATCAGGAGTCACAGACGAGAACTGGACAATTGTCGACTCAGTC
5510 5520 5530 5540 5550 5560 5570 5580 5590 5600
GGTCTGCCCTCAGCTGTGCCTGAGGACAGAGCTGAGCTATCTACCCCTGCAGATTGGAAGCATTACAGGCACTCAAGATCAGCCCTGAAGTGATAAAACC
CCAGACGGGAGTCGACACGGACTCCTGTCTCGACTCGATAGATGGGGACGTCTAACCTTCGTAATGTCCGTGAGTTCTAGTCGGGACTTCACTATTTTGG
5610 5620 5630 5640 5650 5660 5670 5680 5690 5700
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ATTCCGTCTTTAGGTGGTTCTGATCGTCACGGAGGCACAGAGAAGGACACCGACCACCCTTTCTCTCCCCGTCAGGAAGGAACTACGTTCCAGCACACAG
5710 5720 5730 5740 5750 5760 5770 5780 5790 5800
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ATCACCGTGCGAAGGAAGTAAGGGTCACTCTCGTTCACTAGTGGACCCATTCCTTCCAAGTCCACGGACTCGAGCGACCTCTTAAGTAGTGAGTAGGTAG
5810 5820 5830 5840 5850 5860 5870 5880 5890 5900
ACTCTGCTCCTGTAGACATAATCACTTCTGTTGGGTCTTTATAGAGATGATTTATAACTTTGTTGTTTATAGTTTTATGAATGTGTGTATTCATTTAGG
TGAGACGAGGACATCTGTATTAGTGAAGACAACCCAGAAATATCTCTACTAAATATTGAAACAACAAATATCAAAAATACTTACACACATAAGTAAATCC
5910 5920 5930 5940 5950 5960 5970 5980 5990 6000
TCACATGGGAGGTACACATTTTCAGGTGTCTGTCTTTCCATCACACGGGCTTTGAATTAAACTCAGTCTTGGTTTTACCGGCTGAGCCATCTCACCTGCC
AGTGTACCCTCCATGTGTAAAAGTCCACAGACAGAAAGGTAGTGTGCCCGAAACTTAATTTGAGTCAGAACCAAAATGGCCGACTCGGTAGAGTGGACGG
6010 6020 6030 6040 6050 6060 6070 6080 6090 6100
TGATTATTTAAAAATCTCCGGAGTAATCCAGGAGTGTGGTTTATGATTGTAGTATCAACACTCGGGAGGCTGAGGGAGCATCGTTATCATGAGCTCCAGG
ACTAATAAATTTTTAGAGGCCTCATTAGGTCCTCACACCAAATACTAACATCATAGTTGTGAGCCCTCCGACTCCCTCGTAGCAATAGTACTCGAGGTCC
6110 6120 6130 6140 6150 6160 6170 6180 6190 6200
CTAGTTCCAGGCTTGCCTAAGCTGTAGAGCAAGTCACTCTCTTAAAAAGTGCCTCTCCCATATTTTTGTATATAATTTGCATCTGAAATTCTGTTTGCCA
GATCAAGGTCCGAACGGATTCGACATCTCGTTCAGTGAGAGAATTTTTCACGGAGAGGGTATAAAAACATATATTAAACGTAGACTTTAAGACAAACGGT
6210 6220 6230 6240 6250 6260 6270 6280 6290 6300
ATAACTATGAAATTATTCACATTACTAAAATCTTCCTGTGCCAAGTTCTCCAACGAATTAGATCACACTCAGATGAAATGCTAATAAAAATTAAAGCTGT
TATTGATACTTTAATAAGTGTAATGATTTTAGAAGGACACGGTTCAAGAGGTTGCTTAATCTAGTGTGAGTCTACTTTACGATTATTTTTAATTTCGACA
6310 6320 6330 6340 6350 6360 6370 6380 6390 6400
AGCCAGTAGCATGCGTATATTTGGGCTCAGGGCCAACAGGCAGGCGATCTGGGTGTAAGAAAATAGGCTAATGGCTGTGGAATCTGGTCTCTAGTGGCTC
TCGGTCATCGTACGCATATAAACCCGAGTCCCGGTTGTCCGTCCGCTAGACCCACATTCTTTTATCCGATTACCGACACCTTAGACCAGAGATCACCGAG
6410 6420 6430 6440 6450 6460 6470 6480 6490 6500
CGCTGAGAGCTGACCTCAACCACGCTCCCTCAAATTGATTGCCTTCCAGGTTATGATTTCTCATCACAGGAAACTTTGTTGCCCAATTCAAACCCTGTGA
GCGACTCTCGACTGGAGTTGGTGCGAGGGAGTTTAACTAACGGAAGGTCCAATACTAAAGAGTAGTGTCCTTTGAAACAACGGGTTAAGTTTGGGACACT
6510 6520 6530 6540 6550 6560 6570 6580 6590 6600
GTGAAAACAAAAACAGGAGAGCAAGTGCTGCTCCCCGTGCCCCAAAGCCCCTTCTGTCAGGGATCCCAAATGCACCCCAGAGAACAGCTTAGCCTGCAAG
CACTTTTGTTTTTGTCCTCTCGTTCACGACGAGGGGCACGGGGTTTCGGGGAAGACAGTCCCTAGGGTTTACGTGGGGTCTCTTGTCGAATCGGACGTTC

FIG. 15-3

```
        6610      6620      6630      6640      6650      6660      6670      6680      6690      6700
GGCTGGTCCTCATCGCATACCATACATAGGTGGAGGGCTTGTTATTCAATTCCTGGCCTATGAGAGGATACCCCTATTGTTCCTGAAAATGCTGACCAGG
CCGACCAGGAGTAGCGTATGGTATGTATCCACCTCCCGAACAATAAGTTAAGGACCGGATACTCTCCTATGGGGATAACAAGGACTTTTACGACTGGTCC

        6710      6720      6730      6740      6750      6760      6770      6780      6790      6800
ACCTTACTTGTAACAAAGATCCCTCTGCCCCACAATCCAGTTAAGGCAGGAGCAGGAGCCGGAGCAGGAGCAGAAGATAAGCCTTGGATGAAGGGCAAGA
TGGAATGAACATTGTTTCTAGGGAGACGGGGTGTTAGGTCAATTCCGTCCTCGTCCTCGGCCTCGTCCTCGTCTTCTATTCGGAACCTACTTCCCGTTCT

        6810      6820      6830      6840      6850      6860      6870      6880      6890      6900
TGGATAGGGCTCGCTCTGCCCCAAGCCCTGCTGATACCAAGTGCCTTTAAGATACAGCCTTTCCCATCCTAATCTGCAAAGGAAACAGGAAAAAGGAACT
ACCTATCCCGAGCGAGACGGGGTTCGGGACGACTATGGTTCACGGAAATTCTATGTCGGAAAGGGTAGGATTAGACGTTTCCTTTGTCCTTTTTCCTTGA

        6910      6920      6930      6940      6950      6960      6970      6980      6990      7000
TAACCCTCCCTGTGCTCAGACAGAAATGAGACTGTTACCGCCTGCTTCTGTGGTGTTTCTCCTTGCCGCCAACTTGTAAACAAGAGCGAGTGGACCATGC
ATTGGGAGGGACACGAGTCTGTCTTTACTCTGACAATGGCGGACGAAGACACCACAAAGAGGAACGGCGGTTGAACATTTGTTCTCGCTCACCTGGTACG

        7010      7020      7030      7040      7050      7060      7070      7080      7090
GAGCGGGAAGTCGCAAAGTTGTGAGTTGTTGAAAGCTTCCCAGGGACTCATGCTCATCTGTGGACGCTGGATGGGGAGATCTGGGGAAGTATG
CTCGCCCTTCAGCGTTTCAACACTCAACAACTTTCGAAGGGTCCCTGAGTACGAGTAGACACCTGCGACCTACCCCTCTAGACCCCTTCATAC
```

FIG. 15-4

10 20 30 40 50 60 70 80 90 100
CTCGAGGTCCAGTATGGCTTCTCAACCTTCTTGGCAAGAAGGCTGCAGGGACGACCAGGAAGTTTGAAACAGTCTTAGAAGAAAATGCTGGCTTAGAGAC
GAGCTCCAGGTCATACCGAAGAGTTGGAAGAACCGTTCTTCCGACGTCCCTGCTGGTCCTTCAAACTTTGTCAGAATCTTCTTTTACGACCGAATCTCTG

110 120 130 140 150 160 170 180 190 200
AGGTGGCAATGGGGGATGGGGAGCAGTATTCTGGTTTGCATAGAGGCAGAGTCCTTCCAAGTGCTGGGAAACAAGGCAGGAGGGCAGGGATAGAGCAAAT
TCCACCGTTACCCCCTACCCCTCGTCATAAGACCAAACGTATCTCCGTCTCAGGAAGGTTCACGACCCTTTGTTCCGTCCTCCCGTCCCTATCTCGTTTA

210 220 230 240 250 260 270 280 290 300
GATGGCTCTGTATGTGTCCCTGTTCAGTTTGCATTTAATCTGAGCAAAATTTGGCTTTTGACATCTGCAACTCAAAAGAAGGTAATTAGGCAAATGACTG
CTACCGAGACATACACAGGGACAAGTCAAACGTAAATTAGACTCGTTTTAAACCGAAAACTGTAGACGTTGAGTTTTCTTCCATTAATCCGTTTACTGAC

310 320 330 340 350 360 370 380 390 400
ACACATAGATATCTTAATAGTCAAGGAATTTTTTTTTTTTTTTTTGAAGAGTTAGCAGTCAGGGGATGGTAGAAACTGCAAAACCAATCCGTATTCTTTC
TGTGTATCTATAGAATTATCAGTTCCTTAAAAAAAAAAAAAAAAACTTCTCAATCGTCAGTCCCCTACCATCTTTGACGTTTTGGTTAGGCATAAGAAAG

410 420 430 440 450 460 470 480 490 500
TTGAGATTTTTAGACAGTTGATGCTACTAGCCACAAAAAGAGTTTAAGTGGGAGGAGAGTAAGATGCAGGCACCAAGGTGACAGGCTCCAGGTCTGTAG
AACTCTAAAAATCTGTCAACTACGATGATCGGTGTTTTTCTCAAATTCACCCTCCTCTCATTCTACGTCCGTGGTTCCACTGTCCGAGGTCCAGACATC

510 520 530 540 550 560 570 580 590 600
CATTAGCTTACAGATGAGATTCTTTACAGAGAGCCAGGCAGCTGCATTGGCTAAAGCAGATCTGGGAGGGGGCCAGGAGATCAGCTGGCGGCACTCCCAG
GTAATCGAATGTCTACTCTAAGAAATGTCTCTCGGTCCGTCGACGTAACCGATTTCGTCTAGACCCTCCCCCGGTCCTCTAGTCGACCGCCGTGAGGGTC

610 620 630 640 650 660 670 680 690 700
CCTCCAGGAAAGGCAACCCTTATTTCTGGAATTTTAAACTGATAACCCAATTCCCACCAGCCTGGCCAGGCTCTTCCTTAGCTCACATCACAAACACAGA
GGAGGTCCTTTCCGTTGGGAATAAAGACCTTAAAATTTGACTATTGGGTTAAGGGTGGTCGGACCGGTCCGAGAAGGAATCGAGTGTAGTGTTTGTGTCT

710 720 730 740 750 760 770 780 790 800
AGGATTGTTTTAGATGGAGTCATGCTTGATTCTTTCTATACCTACTTCCAAGACCAATTTTATAAAAGTTTATTTACCGCCCGTGTGTGTGTGTGTGTGT
TCCTAACAAAATCTACCTCAGTACGAACTAAGAAAGATATGGATGAAGGTTCTGGTTAAAATATTTTCAAATAAATGGCGGGCACACACACACACACACA

810 820 830 840 850 860 870 880 890 900
GTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGCATGGTATATATGGATGTCAGAGTTTGGTTCTCTCCTTCTGCAGTGGCTCTTAGAGATTGAACTCAGAT
CACACACACACACACACACACACACACACACGTACCATATATACCTACAGTCTCAAACCAAGAGAGGAAGACGTCACACCGAGAATCTCTAACTTGAGTCTA

910 920 930 940 950 960 970 980 990 1000
CATGAGCAAGCACCTTGCTGCCTGCTATGTCCCTCCAGCAGTCTGACCATGTTCCTTCCCCCAAGATTGTGGAAGCTGGACTGAAGATCACAATCTGCCA
GTACTCGTTCGTGGAACGACGGACGATACAGGGAGGTCGTCAGACTGGTACAAGGAAGGGGGTTCTAACACCTTCGACCTGACTTCTAGTGTTAGACGGT

1010 1020 1030 1040 1050 1060 1070 1080 1090 1100
GATGGGCAGAATCTTTACTCTTTGGCACATTTGTTGCTGATGGGGAGTGAATACCCATGGGGACATGGCTGTCATGGTGTGGAAGTGATAGAAATGAAAA
CTACCCGTCTTAGAAATGAGAAACCGTGTAAACAACGACTACCCCTCACTTATGGGTACCCCTGTACCGACAGTACCACACCTTCACTATCTTTACTTTT

1110 1120 1130 1140 1150 1160 1170 1180 1190 1200
CATGTATGGATCTGTCACAGGAGCTGGTGAGGCTGATGGGTGTGTGGGTGGCCACTGTTTGCTCTCTGCTTGTCACAGCCTCTTGTTCAGGGCTTGATCA
GTACATACCTAGACAGTGTCCTCGACCACTCCGACTACCCACACACCCACCGGTGACAAACGAGAGACGAACAGTGTCGGAGAACAAGTCCCGAACTAGT

1210 1220 1230 1240 1250 1260 1270 1280 1290 1300
GGCAGGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGGTCACACCCATCTCAGCAGATCTGTCAGCTTTCCCGCTTTTGTTAGAGGGTG
CCGTCCACACACACACACACACACACACACACACACACACACACACCAGTGTGGGTAGAGTCGTCTAGACAGTCGAAAGGGCGAAAACAATCTCCCAC

1310 1320 1330 1340 1350 1360 1370 1380 1390 1400
ATATCATGCTTCCTGGGGGGAGCTCTGGAAGACAATGAGCAGCCACTTTCCTCTAGATACAATAGGCGGAGTCAGGAAGGTAGTATTGACATTGCTGGGG
TATAGTACGAAGGACCCCCCTCGAGACCTTCTGTTACTCGTCGGTGAAAGGAGATCTATGTTATCCGCCTCAGTCCTTCCATCATAACTGTAACGACCCC

1410 1420 1430 1440 1450 1460 1470 1480 1490 1500
CCTAGGAGCTACTCACTGCTCGGTGGCCGTCAGATGGTGAACCGGCGTAACCTTGGCACACAGGCCTGGGCTGTACAAGGCGTCTGGCTGCAGGGCCAAA
GGATCCTCGATGAGTGACGAGCCACCGGCAGTCTACCACTTGGCCGCATTGGAACCGTGTGTCCGGACCCGACATGTTCCGCAGACCGACGTCCCGGTTT

1510 1520 1530 1540 1550 1560 1570 1580 1590 1600
GAGGACTCCACCCTAGGGACAGGAGTACTTCAGACATCTGGGAATCTGGGATGGGTTTTAAAATTCAGATCCCAATATAAAAAAACAACTCCCAAACAAA
CTCCTGAGGTGGGATCCCTGTCCTCATGAAGTCTGTAGACCCTTAGACCCTACCCAAAATTTTAAGTCTAGGGTTATATTTTTTTGTTGAGGGTTTGTTT

1610 1620 1630 1640 1650
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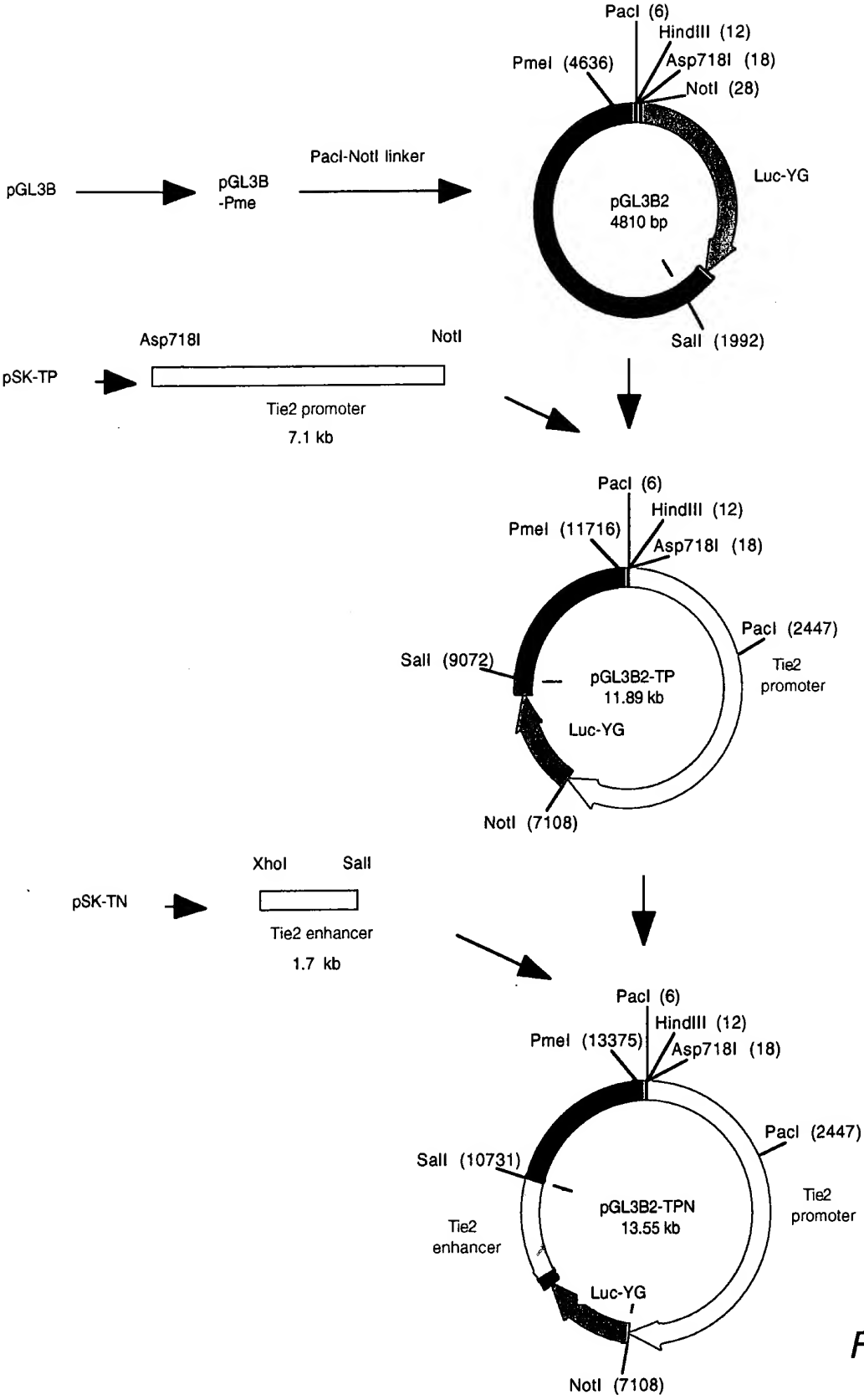
FIG. 16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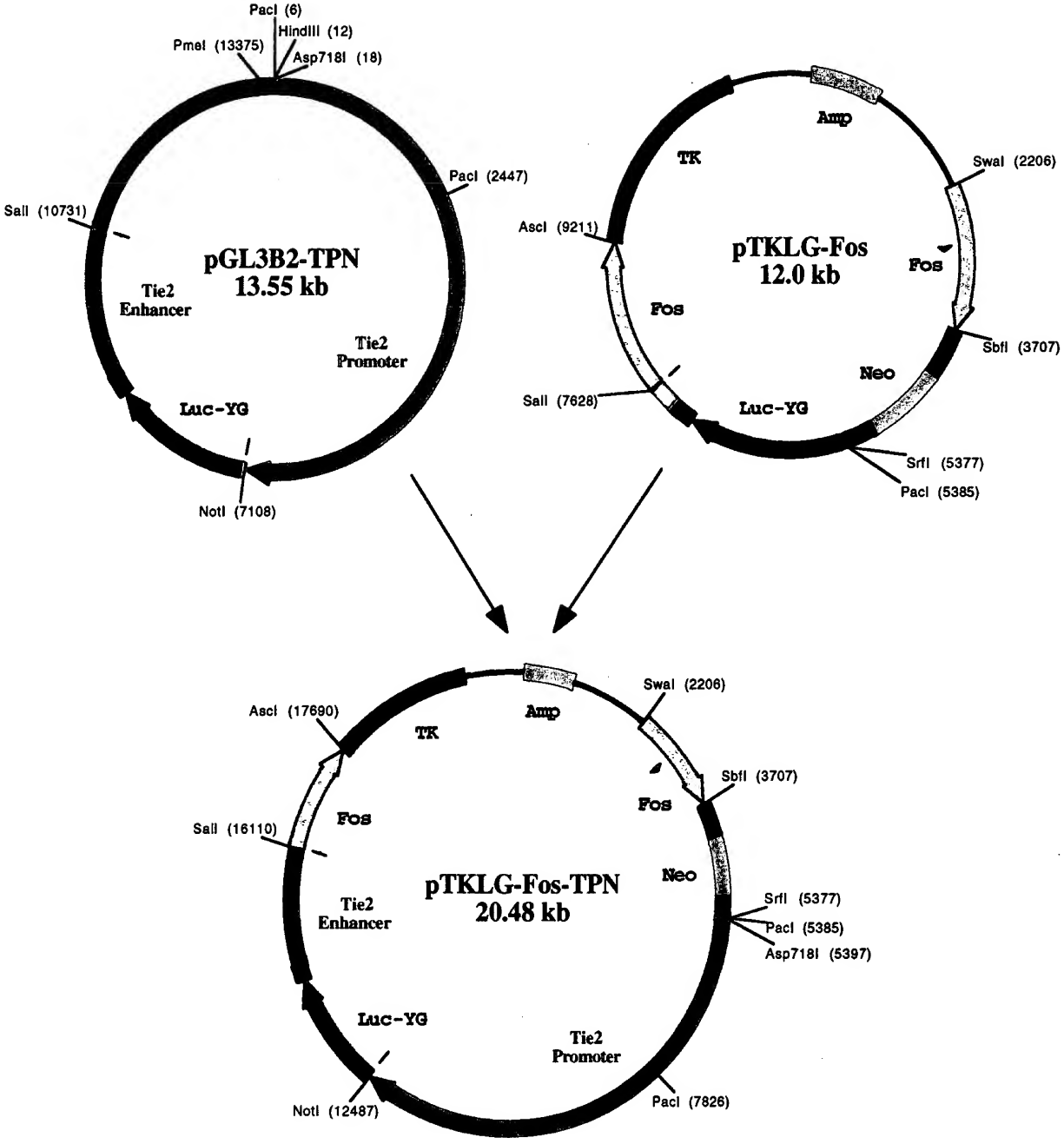
pGL3B
-Pme
PacI-NotI linker
PacI (6)
HindIII (12)
PmeI (4636)
Asp718I (18)
NotI (28)
Luc-YG
pGL3B2
4810 bp
SalI (1992)
Asp718I
NotI
pSK-TP
Tie2 promoter
7.1 kb
PacI (6)
HindIII (12)
PmeI (11716)
Asp718I (18)
PacI (2447)
Tie2
promoter
SalI (9072)
pGL3B2-TP
11.89 kb
Luc-YG
NotI (7108)
XhoI
SalI
pSK-TN
Tie2 enhancer
1.7 kb
PacI (6)
HindIII (12)
PmeI (13375)
Asp718I (18)
PacI (2447)
SalI (10731)
Tie2
promoter
pGL3B2-TPN
13.55 kb
Tie2
enhancer
Luc-YG
NotI (7108)

FIG. 17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HindIII (12)
PmeI (13375)
Asp718I (18)
PacI (2447)
SalI (10731)
pGL3B2-TPN
13.55 kb
Tie2
Enhancer
Tie2
Promoter
Luc-YG
NotI (7108)
Amp
TK
SwaI (2206)
AscI (9211)
pTKLG-Fos
12.0 kb
Fos
Fos
SbfI (3707)
Neo
SalI (7628)
Luc-YG
SrfI (5377)
PacI (5385)
AscI (17690)
TK
Amp
SwaI (2206)
SbfI (3707)
Fos
Fos
SalI (16110)
Neo
pTKLG-Fos-TPN
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Tie2
Enhancer
SrfI (5377)
PacI (5385)
Asp718I (5397)
Luc-YG
Tie2
Promoter
NotI (12487)
PacI (7826)

FIG. 18

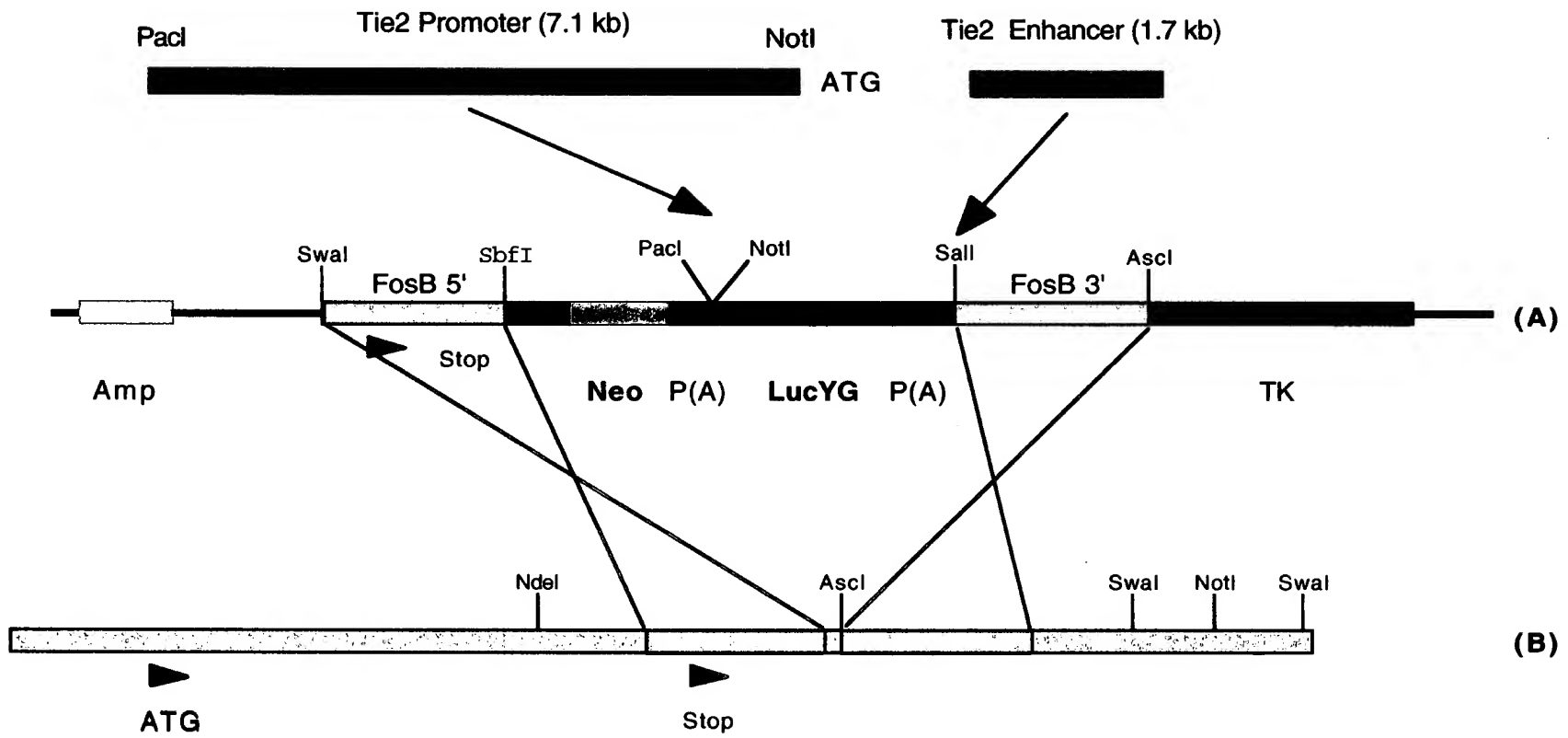

FIG. 19